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ORIGINAL ARTICLES

ON THE LIBERATION OF EPINEPHRIN FROM THE ADRENAL GLANDS*

WITH DISCUSSION OF SOME OF THE METHODS EMPLOYED IN ITS INVESTIGATION

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THE organs which furnish internal secretions are attracting the interest of many physiologists, and among this group of important glands the suprarenal bodies have been the subject of considerable investigation, which has resulted in the accumulation of voluminous literature. From time to time various attractive theories have been formulated, some based upon experimental evidence and others being chiefly speculative, in attempts to solve the problems concerning the functions of these glands. The principal result achieved through these theories is the stimulation of the interest of numerous investigators, resulting in the accumulation of data tending to support one or another of the theories, or, on the other hand, establishing evidence which contradicts the fundamental principles upon which they are based. Some of the prominent theories that have been proposed are as follows: that the adrenal glands neutralize toxins circulating in the blood; that the internal secretion of the glands maintains the normal vascular tone; that the glands are interrelated with other ductless glands, directly and indirectly influencing metabolism; that the adrenals have an emergency function, liberating outbursts of epinephrin in times of special stress in response to emotions such as fear, anger, rage, etc., resulting in the mobilization of the defensive forces through the influence of the liberated epinephrin in the blood and its action on the sympathetic nervous system. However, careful consideration of the literature leads only to the conclusion that we are still far from the solution of the problem concerning the function of the adrenals.

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Out of the mass of experimental work on record, there are but few facts that can be accepted as having been definitely established, and these facts at present lend little, or no support, to any of the existing views of the functions of these glands. With the rapid advance being made in the development of physiologic and biochemical methods of investigation it may be hoped that substantial information will be obtained in due time.

Our knowledge of the function of the adrenal glands begins with the observations made by Addison[1] in 1855, that in the disease, which now bears his name, the adrenal glands are the principal seat of pathologic changes. This was followed by experimental investigations made by Brown-Séquard[2] in 1856, who found that these glands are of vital importance, their complete removal in animals resulting in death. The nature of the material manufactured by the adrenals was investigated by Oliver and Schäfer[3] in 1894, and by Szymonowicz[4] in 1895, by injecting into the circulation of animals, extracts of suprarenal glands. They observed that this caused a marked increase in the blood pressure. Later investigations concerning the adrenals were greatly facilitated by the isolation of an active constituent of the glands, which possesses the same blood pressure raising quality as extracts of the gland. In 1897 Abel[5] obtained an active product from the adrenals (epinephrin), and in 1901 Aldrich[6] and Takamine,[7] independently, isolated an active product (adrenalin). This active principle was prepared synthetically by von Fürth[8] in 1898 (suprarenin), and by Dakin[9] in 1905.

The observations of Lewandowsky[10] and of Langley[11] indicated that the active product of the adrenals produced the same effect upon certain structures which receive nerve supply from the sympathetic system, as is caused by electric excitation of their sympathetic innervation. An extensive study of the actions of adrenalin on various structures or organs was made by Elliott[12] and he showed clearly the sympathomimetic action of this substance. This action of adrenalin led to the use of certain structures, which are innervated through the sympathetic system, as biologic test objects whereby the active product of the adrenal glands can be detected and estimated.

A very delicate means of detecting epinephrin in blood is afforded by the use of segments of rabbit's intestine and uterus. Cannon and de la Paz[13] employed for this purpose strips of longitudinal muscle of cat's intestine. Stewart[14] and Hoskins[15] utilized segments of rabbit's intestine and Stewart showed that it is advantageous to use, as an additional test, segments of the rabbit's uterus. The intestine segment, contracting rhythmically in ordinary (venous or arterial) blood, when brought in contact with epinephrin-containing blood responds by inhibition of the tone and contractions of the segment, while the uterus segment indicates the presence of epinephrin by the opposite effect; i. e., by an increase in tone. The importance of corroborating a reaction produced by a specimen of blood upon the intestine with that shown by the uterus, or some other object which reacts in a different manner than the intestine, is evident, since a number of substances other than epinephrin are capable of causing inhibition of the intestine. In fact, minute changes in the concentration of the salts in the fluid which surrounds the segment or alteration of the oxygen supply may cause inhibition. When the inhibition of the segment is due to epinephrin, it can be con-

firmed by the increase in tone produced when the same specimen of blood is applied to the uterus.

Since the proper interpretation of results obtained with the intestine and uterus segments depends greatly upon the manner in which the test is applied, it is not out of place to describe briefly the method of testing blood upon these objects. The apparatus in which the blood is tested consists of a cylinder, in the bottom of which is a hook for the attachment of the segment. A capillary tube enters the side of the cylinder near the bottom. Through this a constant supply of oxygen is kept bubbling through the liquid which surrounds the test-object; the cylinder is kept in a water-bath at a constant temperature of about 38° C. The segment is attached at one end to the hook in the cylinder and at the other end, by a thread, to a lever which records the contractions. The fluid which surrounds the segment is introduced with the aid of a narrow pipette, properly bent and its end drawn out so that it can enter between the segment and the wall of the cylinder, thus permitting the fluid to be introduced at the bottom of the cylinder, so that, as it enters, it can displace the fluid in which the segment is beating. When the test for epinephrin is applied, the segment, contracting rhythmically in Ringer's fluid, is surrounded by ordinary (usually venous) blood which displaces Ringer's solution as it enters the cylinder. The blood to be tested is then introduced through the pipette at the bottom of the cylinder and as it enters it displaces the indifferent blood and the presence of epinephrin is indicated by an inhibition of the tone and contractions of the intestine segment. A doubtful reaction can always be rendered more certain by applying the test to a segment of the rabbit's uterus. When very small quantities of epinephrin are present in a specimen of blood, the test is facilitated by employing the serum, in which the concentration of epinephrin is greater, instead of the whole blood, for it has been shown that in a blood which contains epinephrin, the serum contains the total amount present in the blood.[16] Some investigators remove one fluid from the cylinder before introducing another. This may be a source of error, as exposure of the segment to the air may alter its sensitiveness in succeeding tests. Also, on removal of one liquid, and then replacing another (or this same liquid), the segment will sink, then be floated up with the emptying and refilling of the cylinder, respectively. This will cause the writing lever to record a rise when the segment sinks, and then a fall as the segment is floated up, which may easily be incorrectly interpreted as an inhibition. Displacing one fluid in the cylinder with another by introducing through the pipette with its orifice at the bottom of the cylinder avoids these possible sources of error. The possibility of incomplete displacement by admixture of the fluids is minimized or completely avoided by introducing more displacing fluid than is necessary to just fill the cylinder. Quantitative experiments made in the course of our work with this method have shown that a given specimen of blood yields constant results when applied in successive observations to the same segment. A large number of observations can usually be made on one segment, but it is important to be certain, when comparing the effects produced by various specimens of blood, that the condition of the segment has not altered. A reaction obtained by one specimen early in the series of observations can not be compared with one obtained by a different specimen later on, unless it can be shown by repeated

applications of different specimens of blood that the sensitiveness of the test object is the same.

Since extracts of the adrenal glands, when introduced into the circulation, are capable of influencing the blood pressure, it is desirable to know whether a substance possessing this activity is given off by the glands to the blood which passes through it. To determine this two means are available: (1) the withdrawal of blood through a cannula from the adrenal veins, and testing it on the biologic test objects, or observing its effect when injected into the circulation of another animal; (2) observations in which the liberation of epinephrin is deduced from changes in the blood pressure or other reactions in one and the same animal, without withdrawing the adrenal vein blood.

Evidence of liberation of epinephrin from the adrenals was first obtained by stimulation of the splanchnic nerves. Dreyer[17] and Tscheboksaroff[18] found that blood collected from the adrenal veins of dogs during stimulation of the splanchnic nerves produces a distinct rise in blood pressure when, after defibrination, it is injected into the circulation of another dog.

Employing rabbits' intestine and uterus segments, it was shown by Stewart[19] that blood collected from the adrenal veins during splanchnic stimulation or during massage of the gland, indicated the presence of epinephrin.

Withdrawal of blood, and its defibrination subject it to possible alteration; therefore, it is desirable to correlate the observations already mentioned with results of experiments made on one and the same animal without withdrawing the adrenal vein blood. Meltzer[20] has shown that when the superior cervical ganglion has been excised in a cat, the pupil on the deganglionated side (which becomes constricted) within a few days becomes especially sensitive to adrenalin, dilating widely when adrenalin is introduced into the circulation, while the normal eye remains unchanged. By means of this reaction, Joseph and Meltzer[21] found that stimulation of the peripheral end of the splanchnic nerve in an animal so prepared caused dilatation of the deganglionated pupil. They explained this on the hypothesis of the liberation of epinephrin from the adrenals into the circulation. Stimulation of the splanchnic in the animal in which the reaction is to be elicited renders it necessary to exclude the possibility that the reaction is a nervous phenomenon due directly to the stimulation of the nerves. Asher[22] attempted to determine this point by excising the abdominal viscera, leaving the adrenals intact, then stimulating the splanchnic nerve with the adrenal veins alternately clamped and open. He studied the effects upon the blood pressure and observed that a rise was obtained when the adrenal veins were open, but when they were clamped no rise in blood pressure was caused by splanchnic stimulation. Employing Meltzer's reaction, previously described, Elliott[23] confirmed Meltzer's observation and also found that in cats this reaction is elicited by splanchnic stimulation when the adrenals are intact but could not be obtained after excision of the glands. He further observed that when one adrenal is excised, stimulation of the splanchnic on that side is without effect, while stimulation of the nerve on the side in which the adrenal is intact causes the characteristic effect upon the pupil.

Further evidence that this reaction is obtained through the liberation of epinephrin into the blood coming from the adrenal glands when the splanchnic

nerves are stimulated or the glands massaged has been found in a number of ways by Stewart, Rogoff and Gibson.[24] It was shown that when blood from the adrenals is prevented from reaching the eyeball, as by clamping the adrenal veins or the vena cava (above the orifices of the adrenal veins) during splanchnic stimulation or massage, no reaction is evoked; but when the clamp is released, the reaction occurs after a time interval corresponding to the circulation time necessary for blood to travel from the adrenal to the eyeball. The time required for this reaction to occur can be varied by variations in the rate of the circulation; i. e., slowing the circulation by vagus stimulation or by hemorrhage causes an increase in the time necessary for the reaction to occur, the difference corresponding to the difference in the rate of the circulation. The reaction evoked by massage or splanchnic stimulation under all of the conditions mentioned can be imitated by injecting the proper amount of adrenalin into the circulation at the level of the adrenals, the time necessary before the reaction occurs corresponding with the circulation time as modified by the conditions interposed. The latent period for the secretion of epinephrin is apparently very short, since the time interval necessary to obtain a given reaction is the same with splanchnic stimulation as when a corresponding amount of adrenalin is injected into the circulation at the level of the adrenals.

The evidence of liberation of epinephrin into the circulation from the adrenal glands in response to artificial stimulation of their splanchnic innervation is conclusive, and the next question to consider is whether it is possible to demonstrate liberation of epinephrin from the glands in the absence of artificial stimulation of their nerves, or what may be termed a "spontaneous liberation."

It was found by Tscheboksaroff[18] that adrenal vein blood collected in the absence of splanchnic stimulation caused a smaller rise in blood pressure, when intravenously injected into another dog, than blood collected during stimulation of the nerves, and that after section of the splanchnic nerves the result indicated a distinct diminution in the adrenalin secretion. O'Connor[25] compared on the frog perfusion preparation (Laewen), the constrictor effects of rabbit's adrenal blood collected before and after section of the splanchnics, and observed a greater vasoconstrictor effect to be produced by the blood obtained before the nerve section. He also showed that shed blood develops vasoconstrictor substances. Trendelenburg[26] further observed that these substances are developed in citrate plasma so rapidly (a fraction of a minute) that the perfusion test for epinephrin when present in small quantities can not be entirely reliable.

It is desirable, therefore, to employ a method which eliminates the obvious difficulties entailed in using shed blood and vasoconstrictor reactions for the tests. A convenient method was employed by us,[27] working with cats and dogs. The blood coming from the adrenal veins was collected in a pocket of the vena cava and then released into the circulation, and simultaneous observations made upon the effects produced on the blood pressure of the animal and the eye reactions of Meltzer. The cava pocket is made by tying off the lumbar and renal veins, and all small branches which enter the cava from the liver to the bifurcation of the iliacs; thus a clamp adjusted just below the liver and one just above the iliacs completes a blind pouch into which only the adrenal veins are emptied. Blood collected in such a pocket is released by removing the upper

clamp and the reactions obtained represent those of unaltered adrenal vein blood. By timing the filling of the pocket and also determining the capacity of the pocket, it is possible with this method to determine the rate of blood flow through the adrenals, and by imitating the reaction obtained when the pocket is released by the injection of proper amounts of adrenalin intravenously, it is also possible to estimate the rate of liberation of epinephrin from the adrenals. It has been shown by this method, with the blood pressure and eye reactions, that in the absence of splanchnic stimulation; i. e., spontaneously, a liberation of epinephrin takes place, varying within narrow limits from 0.0008 to 0.0028 mg. per minute in the cat (or from 0.0003 to 0.001 mg. per kilogram of animal). After section of both sympathetics in the thorax near the diaphragm, including both splanchnics, the spontaneous liberation was no longer detected by these reactions, but section of the splanchnics alone in the abdomen did not always entirely abolish the liberation of epinephrin.*

Electrical stimulation of the peripheral end of the cut nerves during collection of blood in the pocket again elicited the reactions previously obtained. The same result was obtained when the pocket blood was tested upon rabbit's intestine and uterus segments.[28] As the adrenal vein blood, when the segment test is applied, is not diluted with the general blood, as is the case with the test described, these test objects are capable of detecting smaller amounts of epinephrin in the pocket blood than could be detected by the blood pressure or eye reactions. The question may be raised whether this is a normal liberation, or is due to the experimental conditions (trauma, anesthesia, etc.). Although some authors seem to assume that trauma and other experimental conditions will necessarily increase the spontaneous liberation, no experimental proof of this has ever been given. The fact that the output, as experimentally determined, varies within rather narrow limits in different cats, notwithstanding differences in the degree of trauma and the nature and depth of anesthesia, is much in favor of the view that the liberation is a normal phenomenon. We have shown that the anesthetic has nothing to do with it; for (a) the output of epinephrin is within the ordinary limits when anesthesia is produced without the use of a chemical anesthetic, as by a pressure bag inserted intracranially; (b) in animals whose spinal cord has been severed, in the cervical region, some days before the experiment and in which, accordingly, no anesthetic was necessary for testing the adrenal vein blood, the output was also within the usual limits.

It has been established beyond doubt that the adrenal glands continuously secrete a certain normal amount of epinephrin, and that electric excitation of their nerves causes liberation of epinephrin to take place. This leads to the question whether certain physiologic processes are capable of influencing the quantity of epinephrin liberated from these glands.

It has been stated by some writers that the adrenal glands are stimulated to increased secretion of epinephrin by such influences as asphyxia, stimulation of sensory nerves,[29] emotional disturbances[13] and by the introduction into the

*It is known that all of the secretory fibers to the adrenals do not come from the splanchnic nerves, some of them being given off from the sympathetic lower than the origin of the splanchnics. If there is still a detectable liberation of epinephrin, after section of nerves to the adrenals, some of the nerves going to the glands must have escaped section. In the entire absence of innervation, the adrenals do not liberate epinephrin, and do not seem to regain this power, while the formation is apparently not interfered with after section of the nerves. It must be assumed that after the store, in the glands, has been replenished, the formation stops.

circulation of certain gland extracts.[30] The experimental evidence offered as proof of such an effect upon the adrenal glands is not substantial, as it is based upon investigations made with methods which can not yield reliable results.

For these investigations, blood was collected, with the aid of an aspirator, from the inferior vena cava at the level of the adrenals, by inserting a flexible catheter through an incision in the femoral vein (in cats) so that the opening in the end of the catheter was just anterior to the orifices of the adrenal veins. Specimens of blood were obtained through the catheter before and after causing asphyxia, etc., and were tested for epinephrin on intestine strips or segments. Inhibition of the test object caused by applying the specimen of blood collected after the experimental condition was induced was interpreted as indicating an increase in the amount of epinephrin liberated from the adrenals. It must be pointed out that only the intestine was used as a test object and, as previously stated, this test can be considered reliable only when it is possible to confirm the reaction by some other test object. Indeed, Cannon and Hoskins[29] state that ordinary venous blood collected from an animal during asphyxia causes inhibition of the intestine segment, although they show that this is not due to epinephrin. This fact has been repeatedly observed in the course of our work in this laboratory, and with the aid of the uterus segment we have always been able to eliminate the possibility of such a reaction being due to epinephrin, as it also caused inhibition of the tone of the uterus, while epinephrin has the opposite effect on this test object.

If the blood collected through a catheter from the adrenal level causes an inhibition of the intestine which is due to the presence of epinephrin, this yields no information on the rate of liberation of epinephrin from the adrenals. For this, it is essential to know the rate of the blood flow. A high concentration of epinephrin in the blood may be accompanied by a correspondingly slow blood flow through the adrenal or through the cava, while the liberation of epinephrin from the gland remains constant. It has been shown[31] that within a wide range of variation of blood flow through the adrenals the liberation is approximately constant, and that the concentration of epinephrin in the adrenal vein blood varies inversely with the rate of blood flow through the glands.

It is conceivable that changes in the circulation induced during asphyxia, etc., are capable of sufficiently altering the rate of the circulation in the inferior cava to alter the concentration of epinephrin in the blood which is collected from the cava near the adrenals, but this is not an indication that any change in the rate of liberation of epinephrin from the adrenals has taken place.

Although we have recognized that the catheter method can not yield substantial information, we have made experiments, with this method, on the influence of emotions, asphyxia, and afferent stimulation on the liberation of epinephrin, and have been unable to confirm the results that have been reported.

We have studied the influence of asphyxia and sensory stimulation (of large nerve trunks) upon the liberation of epinephrin from the adrenals,[27] employing the "cava pocket" previously described, with the blood pressure and eye reactions. No effect upon the rate of liberation could be detected by this method. The same result was obtained with the adrenal vein blood, obtained from the cava pocket when tested upon rabbit's intestine and uterus segments.[32, 33] These

observations permitted the study of the rate of blood flow through the adrenals, as well as the concentration of the epinephrin in the adrenal vein blood, and any increase in the concentration could always be accounted for by a corresponding diminution in the rate of blood flow, indicating that no detectable change in the rate of liberation from the glands had taken place during asphyxia or stimulation of the sensory nerves.

Cannon[34] has reported, in a preliminary communication, that he has devised a new method whereby he believes an increased activity of the adrenal is evidenced during asphyxia by a rise in blood pressure which he fails to obtain when the adrenals are excised. The recent observations of Gley and Quinquaud,[35] however, indicate that the rise in blood pressure during asphyxia does not depend upon secretion of epinephrin from the adrenals, for they find no diminution in the rise with asphyxia after ligation of the suprarenal veins. This is against the idea that asphyxia causes any sensible increase in the rate of liberation of epinephrin.

The influence of certain drugs in diminishing the content of epinephrin in the adrenals has led Elliott[23] to interpret the diminished store as due to an increase in the liberation of epinephrin from the gland. He concludes that since morphine, in the cat, produces effects which simulate the general appearance of fright, the resulting diminution of epinephrin store in the adrenals must be due to the increased liberation of epinephrin from the glands in consequence of the emotional excitation or "morphine fright," although he did not directly study the influence of frightening the animals. The effect of morphine in depleting the store of epinephrin from the adrenals has been confirmed by us.[36] But it has been shown that this effect has nothing to do with the emotional state of the cat, since in the dog and rabbit morphine also depletes the epinephrin store from the gland, although the physiologic picture of the animals is the opposite of that in the cat, the narcotic action being manifest. It must be emphasized that diminution of the store of epinephrin in the gland can not be assumed without proof to be the result of increased liberation, as the epinephrin content of the adrenals at any time can only represent the balance between production and liberation. If the rate of production is lessened, the store may be diminished without any change in the output. And contrariwise, if the production is increased, the rate of liberation may also be increased without any diminution in the store. For example, a considerable amount can be caused to be liberated by electric excitation of the splanchnics without noticeable influence on the store of epinephrin in the gland.[24, 36]

There is at present no obvious method by which the influence of emotions upon the rate of liberation of epinephrin from the adrenals can be properly studied. It is not permissible to assume that the symptoms of sympathetic excitation which are seen in a frightened animal must be due to the action of epinephrin liberated in large amounts from the adrenal glands, for the same symptoms can be elicited in animals so prepared that very little or no epinephrin is being given off from the adrenals. By excision of one adrenal and denervation of the opposite gland in the cat it has been shown that the animal can live indefinitely in apparently excellent health, although the operation has reduced the epinephrin from the adrenals to a very small fraction of the normal, and in

many cases to quantities too small for detection with extremely sensitive test objects, indicating practically no liberation whatever.[28] In some of the cats it was found that the liberation of epinephrin from the adrenals was so interfered with by this operation that there could not have been one-thousandth of the normal liberation, if any epinephrin was being given off from the glands. These animals, nevertheless, responded readily to fright and other emotional disturbances with the usual symptoms of sympathetic excitation, in the same manner as normal cats. Certainly, an outburst, through nervous influence, of epinephrin in such quantities as would be necessary to produce these symptoms would be impossible in these animals.

The conception of an emergency function of the adrenal gland lacks substantial evidence. It involves essentially the occurrence of sudden outbursts of epinephrin far above the normal amounts liberated. It has not been shown that the liberation of such amounts of epinephrin can be induced. Even if it could be proved that during such emergency conditions the adrenals responded with augmented liberation, the suggestion that this has a bearing upon the emergency mobilization of sugar in the body, as evidenced by hyperglycemia[37] is not tenable, since it has been shown that cats so prepared that the liberation of epinephrin from the adrenals is reduced to quantities too minute for detection are still capable of responding to the usual procedures (asphyxia, etherization, etc.) employed in producing experimental hyperglycemia.[38] The normal blood sugar in these animals was the same as that found in unoperated animals. This is against the idea of the existence of a hypoglycemia due to adrenal deficiency (said to exist after adrenalectomy, in which the animal is moribund). Further evidence against the view that these hyperglycemias are associated with an increased liberation of epinephrin from the adrenals, or that they are similar to the hyperglycemia produced by injection of adrenalin, is the well-known fact that subcutaneous injection of adrenalin causes hyperglycemia more readily than intravenous introduction.

Animals, with practically no epinephrin being given off from their adrenals, as previously stated, are capable of responding to fright, rage, fear, etc., in the same manner as normal animals. They seem to be as capable of muscular exertion and as combative as the normal animals. The fact that such cats live indefinitely in apparently good nutrient condition suggests that epinephrin is probably not indispensable to life and health, unless the retroperitoneal and other chromaffin tissue in the body, which has been shown to contain epinephrin,[39] can compensate for the loss of epinephrin secretion from the adrenals. It has not been shown, however, that such chromaffin tissue liberates epinephrin. It is possible that some other substance, at present unknown, the liberation of which is under nervous influence, may be found in the secretion of the adrenals, the lack of which is responsible for loss of life when the adrenals are extirpated.

A number of writers have attempted to show that the secretion of epinephrin from the adrenals is influenced by shock. Some of the conclusions offered are based upon histologic appearance of the glands, indicating a loss of chromaffin substance. This can not be taken as evidence of an increase in the liberation of epinephrin, for the same reason discussed previously in relation to conclusions based upon a decrease of epinephrin store in the glands; nor is it likely that his-

tologic examination of the glands could yield definite quantitative information.

An investigation in which adrenal vein blood was collected before and after induction of shock and the bloods tested upon intestine segments was reported by Bedford.[40] He concludes that the rate of liberation of epinephrin from the adrenals in dogs is augmented by shock produced in several ways. The tracings accompanying the paper do not indicate in what manner the test objects were subjected to the action of the bloods. No satisfactory estimations were made to determine quantitatively the amount of epinephrin in the adrenal vein blood collected before and after shock was induced. On careful consideration of the results reported, the only definite information that can be gathered is that if the inhibitions of the intestine were due to epinephrin in the bloods tested, the specimens collected after the induction of shock had a higher concentration of epinephrin than the specimen collected before shock was induced. This increased concentration seems to correspond closely with a fall in the blood pressure. As already pointed out, it is to be expected that in a condition of low blood pressure, when the rate of blood flow through the adrenals is markedly slowed, there will be a relative increase in the concentration of epinephrin in the adrenal blood, although the rate of liberation may be unaltered.

In view of the fact that the adrenal glands secrete a substance so potent as epinephrin, and since it has been shown that the liberation of this secretion into the circulation is sustained through the influence of nerves which are in connection with a definite center in the spinal cord,[41] it would seem not unlikely that certain experimental procedures, such as asphyxia, stimulation of sensory nerves, etc., might be capable of influencing the liberation of epinephrin, reflexly, through this center. This must not be assumed as a fact, however, until it is proved.

Premature attempts on the part of clinical men to apply what is at present known of the physiology of the adrenals, at least when risk to the patient is involved, are to be deprecated. Certainly, the present state of our knowledge of the subject does not warrant its clinical application to the extent of attempting adrenalectomy as a measure of relief in conditions of arterial hypertonus associated with Bright's disease, on the assumption that this condition is associated with hyperadrenalinemia, as has been done.

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THE RESPONSIBILITY OF THE VACCINATOR IN OVERCOMING THE RATIONAL OBJECTIONS TO SMALLPOX VACCINATION*

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EDWARD JENNER published his "Inquiry into the Causes and Effects of Variolæ Vacciniæ" in 1798. Two years later, smallpox vaccine was brought to this country, and Waterhouse of Cambridge, Massachusetts, performed the first American vaccination on his son, aged five years. By 1803, the practice of vaccination had spread throughout Europe and a ship had been dispatched to carry "the blessed vaccine" to the Spanish possessions in the Old and New Worlds.

In contrast to the remarkable support which the new discovery received throughout the world, we find an antivaccination propaganda based on the belief that those inoculated with cowpox would assume bovine characters and features. In a pamphlet entiled "Cowpox Inoculation no Security against Smallpox Infection," a Doctor Rowley makes the following statement: "Various beastly diseases common to cattle have appeared among the human species since the introduction of cowpox—cowpox mange, cowpox abscess, cowpox ulcer, cowpox gangrene, cowpox mortification, and enormous hideous swellings of the face, resembling the countenance of an ox with the eyes distorted and the eyelids forced out of their true situation. Smallpox is a visitation from God, but the cowpox is produced by presumptious man; the former was what Heaven ordained, the latter is, perhaps, a daring violation of our holy religion."

In an age when "laudable pus" accompanied almost every surgical operation, it is not remarkable that many severe infections followed vaccination, especially if the large scarifications, so vigorously condemned by Jenner, were used. The superstition of the transmission of animal characters is very old and finds a present-day echo in the statement that the victim of rabies "barks like a dog." It is not customary in this generation to blame an offended deity for private and public calamity, but many people, misguided by popular advertisements, are pouring libations in the form of disinfectants into the garbage can and house plumbing, thinking thereby to purchase immunity from disease. These are the people who say that smallpox has decreased because of better sanitation.

Setting aside the unscientific objections to vaccination, which have only slightly changed their characteristics in the past century, let us consider the rational objections to vaccination, which we find even among persons medically orthodox. These objections are two in number and the responsibility for their continuance rests squarely on the medical profession.

THE USE OF SMALL MULTIPLE SCARIFICATIONS

The first objection to vaccination is that it is dangerous since it is often

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accompanied by a secondary infection which results in a slowly granulating ulcer and a disfiguring scar. In a previous communication,[1] we have shown that "the prevention of secondary infection following smallpox vaccination depends essentially on the use of small multiple scarifications which, when inoculated, give rise to small vesicles which are not easily broken, and do not foster anaerobic conditions and a central slough." The large unsightly vaccination scars so commonly seen are due to the slow healing of an ulcer produced by the inoculation of a large cross-scarified area. *The vaccine colony grows only in unbroken skin.* It is obvious, therefore, that vaccinators should emply the smallest scarification consistent with the implantation of the vaccine on the derma. It is our custom to remove three small circles of epidermis by the rotation of a chisel having a 2.0 mm. cutting edge, but excellent results are obtained by short scratches made at least 2.0 cm. apart with an ordinary sewing needle. Hill[2] advocates placing a drop of vaccine on the skin, and carrying a small portion through to the derma by acupuncture. As long as small scarifications are used, neither the method of vaccine preparation, the bacterial content of the vaccine, or the use of antiseptics on the resulting vesicle will influence the course of a primary vaccinia.

REPEATED FAILURES TO SECURE SUCCESSFUL VACCINATION ARE NOT EVIDENCES OF IMMUNITY

The second and more serious objection to vaccination is that it does not protect against smallpox. As early as 1804, Jenner was forced to admit that smallpox could occur in persons who had previously been vaccinated, though he believed that the failure to secure immunity was the result of improper technic. The presence of a large irregular scar following vaccination is only slightly better evidence of immunity than its continual absence after repeated unsuccessful attempts to vaccinate. In the first instance the scar may be the result ot an infective process which has destroyed the vaccine organism before immunity has been produced, and in the second instance the failure to produce a vaccinia may be due to the lack of potency in the vaccine employed.

The practice of issuing vaccination certificates based on a "guess" that the subject is immune because, one, two, or three vaccinations fail to take is almost as potent for evil as improper vaccination technic. Every year we produce primary vaccinias in persons with a history of from one to four or more failures previous to entering the university (Table I). Every year we produce primary vaccinias in persons with a history of having recently swallowed "variolin" pills. Experiences of this sort have bred within us an intense skepticism concerning vaccination certificates unaccompanied by vaccination scars. We do not question the motives behind the issue of these certificates to the scarless, but our experience shows that persons with and without vaccination scars are constantly being declared immune where no immunity exists. As shown in Table II, only 51 (38 per cent) of 136 persons whose vaccination scars were more than twenty years old gave evidence of immunity on revaccination, while 46 (14 per cent) of 318 persons whose vaccination scars were less than ten years old gave unmodified vaccinias. If these people get smallpox, there is more

fodder for the nourishment of the antivaccination propaganda. Who is to blame for this condition if not the man who "guesses" that his patient is immune? Among our previously unvaccinated intrants with no history of smallpox, we have 100 per cent of vesicle formation on vaccination. We have yet to see our first natural immune. We do not believe that he exists. Repeated vaccination with an inert vaccine will occasionally render the subject immune to potent vaccine. These persons present no vaccination scar, but show a well-marked reaction of immunity on revaccination. On the other hand, a failure will be characterized by the absence of any reaction at the vaccination site other than that due to scarification trauma. True failures furnish valuable checks on vaccine potency.

Inquiry at the laboratory, following 23 failures with a certain vaccine disclosed the fact that the air used in driving the ether out of this vaccine had been accidentally saturated with a chemical fatal to the vaccinia organism. Brooks[3] reports failure of vaccine to act in two hundred persons in Oxford, New York, during a smallpox outbreak in 1915. This failure was traced to contact with steam pipes during the transit of the vaccine.

In order to test the effect of age, method of preparation, and method of storage on the potency of vaccine, we conducted a number of vaccinations with vaccines of various ages prepared by various methods.

In a series of vaccinations made with vaccines ground in glycerine and stored in the ice box for varying periods before use, there were eight reactions and no failures at the end of six months storage; eight reactions and one failure at the end of five months; eighteen reactions and one failure at the end of four months; twenty-four reactions and one failure at the end of three and one-half months; one hundred seventy-eight reactions and one failure when the vaccine had been stored for five weeks; and thirty-three reactions with no failures when the vaccine had been stored two weeks before use.

In a similar series made with a glycerinated vaccine which had in addition been subjected to the action of ether to reduce the number of contaminating organisms before storage in the ice box, there were eight reactions and one failure with vaccine six months in storage; two reactions and four failures with vaccine held five months; nineteen reactions and no failures with vaccine held four months; and fourteen reactions with no failures with vaccine held three and one-half months. The percentage of failures in this series is only slightly higher than with the corresponding glycerinated vaccines which had not been etherized.

In a series of 230 vaccinations made with a vaccine which had been etherized but showed a high bacterial count there were no failures; but equally good results were obtained in 168 vaccinations with a vaccine which had been etherized until practically sterile.

In thirty-eight vaccinations with a vaccine which had been incubated for twenty-four hours after grinding in glycerine and then stored in the ice box until practically sterile, there were no failures.

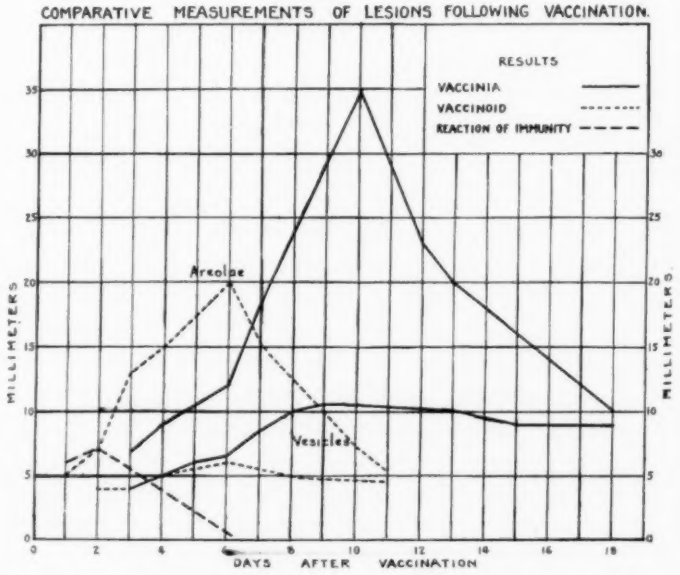
A series of sterile vaccines prepared according to the method of Noguchi,[4] by passage through rabbit testicles, resulted in five reactions and four failures

on second passage of the strain originally received from the Rockefeller Institute; ten reactions and eleven failures on the fifteenth passage; and seven reactions and fifty-six failures on the twenty-ninth passage through rabbit testicles. This shows a steady deterioration which Greely[5] believes to be due to the absence of certain spore-like forms of the organism which are present in vaccine cultivated on the skin.

The results of these vaccinations show that the greatest factor in vaccine potency is the maintenance of ice box temperature during the entire period between manufacture and use. Etherizing and preliminary incubating do not appear to affect the potency provided the vaccine is properly iced. On the other hand, failure to secure constant ice box conditions will result in the use of large amounts of inert virus even if the expiration date is not exceeded. With

CHART 1

COMPARATIVE MEASUREMENTS OF LESIONS FOLLOWING VACCINATION.



no check on the potency of the vaccine, it is obviously absurd to issue a certificate that the vaccinator has used due diligence and can not produce a successful vaccination.*

COMPARISON OF THE THREE TYPES OF SUCCESSFUL VACCINATION

Depending on the response of the subject to the invading vaccine antigen, we are able to distinguish three forms of successful vaccination. When antibodies are present in the tissues, the invading organisms are at once destroyed. This reaction of immunity is characterized by an areola which appears within twenty-four hours after the vaccination and fades out without developing into a vesicle.

*Since the above was submitted for publication, I have observed two true failures in previously unvaccinated persons, with a vaccine three months old, obtained from an establishment whose product we have found to give uniformly good results when six months old. In the first instance the vaccine reached our icebox via an Army Supply Depot, and in the second it was transferred from the manufacturer's icebox directly to ours. This emphasizes the need for icebox or vacuum bottle conditions *at all times* from establishment to arm.—J. N. F.

Inert vaccine may produce the reaction of immunity in an immune subject, or even a slight papule on the fourth or fifth day in a nonimmune subject. When antibodies are no longer present but the ability to quickly form them still exists, the growing colony of vaccinia organisms is arrested and destroyed before it reaches its full development. In consequence, on the fifth day following vaccination this secondary vaccinia (vaccinoid) is characterized by a larger areola and a smaller vesicle than a primary vaccinia of the same age.

The characteristics of the three types of successful vaccination may be shown by plotting the daily average measurements of the lesions of a series of vaccinas with corresponding measurements of a series of vaccinoids and a series ot reactions of immunity (Chart I). The vaccination certificate issued by this university does not provide for vaccination failure. The reaction of immunity is a successful vaccination because the act of calling out antibodies to produce this reaction brings up immunity to its maximum. Smallpox immunity is like a clock: the further it has run down the longer it takes to wind it; but it can only be wound to a certain point no matter where you start winding. Producing the reaction of immunity is like winding an eight-day clock which has only run one day since the previous winding. You would not say that you had failed to wind the clock because you had to stop after one or two turns of the key.

The secret of our 100 per cent of vesicle formation in the previously unvaccinated (Table I) is simple. It consists in the two words "fresh" and "cold" applied to the smallpox vaccines. Fresh because it is the very latest released by the manufacturer, cold because it is barely half an hour from his ice box to our ice box and is kept in cracked ice while in the vaccination room. Any vaccinator who will buy his smallpox vaccine in bulk, have it shipped in a vacuum bottle to avoid possible steam pipe episodes, and keep it at ice box temperature after removal from the vacuum bottle, has a right to demand 100 per cent of vesicle formation in the previously unvaccinated. If one of these subjects gives a reaction of immunity on first vaccination, you may rest assured that smallpox has been there before you.

TABLE I.

RESULTS OF VACCINATION OF UNIVERSITY OF CALIFORNIA INTRANTS DURING THE ACADEMIC YEAR 1916-17 CLASSIFIED ACCORDING TO VACCINATION HISTORY.

	PRIMARY VACCINIA		SECONDARY VACCINIA (VACCINOID)		REACTION OF IMMUNITY	
	NO.	%	NO.	%	NO.	%
Scar absent						
Previously unvaccinated	178	96	8	4		
History of smallpox	7	24	11	38	11	.38
History of ingestion of "variolin"	2	100				
Previously vaccinated but no scar						
once	145	92	10	6	2	2
twice	37	92	2	5	1	3
three times	24	86	4	14		
four times or more	29	88	3	9	1	3
Scar indistinct	16	52	10	32	5	16
Scar distinct	7	12	28	39	30	49

TABLE II.

RESULTS OF THE REVACCINATION OF 898 PERSONS SHOWING VACCINATION SCARS.

AGE OF SCAR	PRIMARY VACCINIA		SECONDARY VACCINIA (VACCINOID)		REACTION OF IMMUNITY	
	NO.	%	NO.	%	NO.	%
Under 10 years	46	14	121	38	151	48
10 to 20 years	61	14	171	38	212	48
Over 20 years	48	35	37	27	51	38

CONCLUSIONS

1. The use of small multiple insertions will shorten the course and minimize the dangers of smallpox vaccination.

2. Properly cooled smallpox vaccine produced a high percentage of successful vaccinations four, five, and six months after collection.

3. The best results were secured with vaccine used within one month after collection.

4. Vaccine prepared according to the method of Noguchi, while bacteria-free, seems impracticable for commercial use on account of rapid deterioration.

5. Since the object of vaccination is to secure immunity, successful vaccination consists in producing either a primary vaccinia, a secondary vaccinia (vaccinoid), or a reaction of immunity (Chart I).

6. All vaccination certificates should be based on actual evidence of immunity as indicated by one of the three reactions described, and not on repeated failures to secure a typical vaccinia.

7. There will be no vaccination failures if cold, fresh, potent smallpox vaccine be used.

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WAR DEAFNESS AND ITS PREVENTION—A REPORT OF TESTS UPON EIGHT PREVENTIVES*

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THE object of the series of experiments here reported was to test the relative efficiency of various devices for preventing injuries to the ear parts by detonations. Eight preventives have been used in the work done to date; as others are obtained they will be tested in similar manner.

PREVENTIVES USED IN TESTS

The first two devices were sent to me by Major V. C. Vaughan, of the National Research Council, with the request that I try them out and report. They had been submitted to the Council by the inventors.

1. The "Scientific Ear Drum Protector 'Tommy,'" patented in Great Britain and France in 1915, manufactured by Geo. F. Berry, 4 Cullum Street, Fenchurch Street, London, E. C. It consists of a hollow soft rubber spherical bulb with an opening on one side surrounded by a flange. The external diameter of the spherical part is about 9.5 mm., and of the flange 11.5 mm. A pair in an envelope with a short rod for helping to insert them properly retails at one shilling.

2. A device invented, according to the letter from Major Vaughan, by Dr. J. Gordon Wilson, Professor of Otology at Northwestern University, and at present in the medical corps of the British army, and Professor A. A. Michelson, of the Physics Department of the University of Chicago. The device consists of a hollow framework of hard rubber in which is supported a valve of light metal so arranged as to stay open and permit ordinary sounds to pass at the edges, but so adjusted that detonation waves can cause it to shut by moving inward and forming contact with what may be called the valve-seat. The outer end is covered by a fine meshed wire gauze placed in a detachable metal cap. The large end is 17 mm. in diameter; the small end is 8 mm. at the center of a slight bulge near the end. This inner end is too small to fit any of the meatus I have tried it in, but this is a matter easily remedied. It is probable, judging from the fact that the end is small and that one of the two instruments sent was embedded in a cast of plaster of Paris made to fit some person's right ear, that the intention was to fit each user individually by making casts for each.[1] This would certainly be difficult, if not impracticable, to carry out successfully in an army, for the casts would require frequent renewal. Two other serious objections are evident on critical consideration of this instrument. In field service, especially in trench life, with its mud and other dirt, no wire gauze would be able to prevent particles of material from passing and a very small particle would be sufficient, when caught under the edge of the valve, to hold it open permanently. The second

*From the Department of Anatomy, University of Michigan Medical School, Ann Arbor, Mich. A previous paper on this subject may be found in this Journal, ii, 849.

[1]The device submitted in a cast does not open into the external meatus, but is so placed that it must have rested against the concha just posterior to the orifice of the meatus.

objection is the one I raised in the previous article as being common to all hard obturators; namely, that bullets passing alongside the head and wounding only the pinna or the outer part of the external meatus, in themselves relatively slight wounds and of quite common occurrence, would shatter the hard parts of an obturator present and form secondary projectiles of the fragments, causing much more severe wounds. A further theoretical objection is that there is nothing to prevent the air in the meatus from passing out during the rarefaction phase following the condensation phase of the detonation wave; the valve acts only in one direction. This would permit injury due to the air contained in the middle ear cavity, the eustachian tube not being open normally except during part of the swallowing act.[2]

The next two devices were obtained by direct purchase from the manufacturers.[3] For a description and critical discussion of them and the following preventive measures the reader is referred to the previous article.

3. The Elliott "Perfect Ear Protector," manufactured by J. A. R. Elliott, P. O. Box 201, New York City.

4. The "Mallock-Armstrong Ear Defender," 1916 pattern, manufactured by the Mallock-Armstrong Ear Defender Co., 2, Palmer Street, Westminster, London, S. W. This 1916 pattern differs from the description of the device given in the previous article in that the diaphragm between the wire gauzes is not of metal, as the 1915 patent claims call for, buf appears to be of a membranous nature, and is translucent. The device is now made in seven sizes instead of four, to enable more exact fitting. The price has been advanced from three shillings to four shillings a pair.

5. Wax cones which I have made after the description given by Rho as having been adopted in the Italian navy.

6. Dry cotton, placed firmly.

7. Cotton saturated with glycerine, carefully kneaded to drive out all the air bubbles possible. Before using, the excess glycerine was squeezed out with the fingers.

8. Cotton saturated with vaseline, carefully worked in until a uniform mass was obtained.

METHOD OF TESTING

The mechanical devices are made only of a size to fit human ears, and so the ideal manner of testing them is upon human subjects, which will be, of course, the final test of efficiency. But for laboratory tests, in which autopsies and histologic preparations are desired, animals must be used. To do this, it was necessary to devise some new apparatus. To have used a plain piece of tapering glass tubing drawn to a size at one end suitable for fitting the meatus of the animal used and large enough at the other end to receive the various devices would have been the simplest way, but a very serious objection is met with due to the fact that the consistency of the glass differs so much from the pliable human ear that

[2] I wish at this place to express my great admiration for the work of both Prof. Michelson and Dr. Wilson in their chosen fields; I have hesitated to express criticisms of their instrument, especially so since mechanics is not my own field.

[3] I ordered also three pairs of the Rogers Plastic Ear Plugs, described in the previous article, but have not yet succeeded in obtaining them, though they were ordered from London in June.

a fair test of the holding power of the preventives would not be given. A plain piece of rubber tubing attached to the glass tube simulates the consistency well enough, but not the shape of the part of the human external ear in which the devices are intended to fit. Two of the devices, the "Tommy" and the Elliott protector, have flanges which fit beautifully over the end of a piece of tubing, but not so well in the actual ear, where the anterior wall of the meatus is continuous directly with the posterior surface of the tragus, while a "shoulder" is present at the posterior part of the orifice. The idea was conceived, after trials with these other things, of trying to make a holding device of soft rubber of the shape of the concha and first part of the meatus of a human ear. Such a device would, if made with sufficiently thick walls, be of a consistency simulating the human ear in the part holding the devices, and would, therefore, give a better test of them. Being inexperienced in working with rubber, I consulted Dr. E. L. Whitman, Instructor in Dental Technics in the Dental School of the University. He said that my idea could be carried out, and I was able to interest a dental student, Mr. G. C. Lubke, who made for me two rubber "ears," which answer the requirements very well. These were built over a plaster cast made of an ear of a cadaver. A short extension of the outer part of the meatus in the form of a very heavy walled rubber tube, built as an integral part of the device, provides a means of fastening a glass tube for connecting to the external meatus of animals.

Glass tubes may, of course, be made to fit any animal it is desired to use, being simply glass tubing drawn, or blown, to the shape and size needed. For guinea pigs, which I have used in these experiments, I made several of these plugs of varying sizes. The one which I like best after experience with them is 17.5 mm. long, and has an internal diameter of 6 mm. at the large end, tapering to 3.5 mm. at the smallest part. The small end was flanged slightly in making, so that the 3.5 mm. diameter is about 1 mm. from the end. This tube does not pass into the meatus of a guinea pig, but fits over the orifice, and in order to completely close any small openings left a soft wax was used. This was made by mixing beeswax and vaseline in about equal parts by heating. The wax was packed about the glass tube and built up in such a way that it formed a wall that continued the outer surface of the rubber and extended to the side of the head of the animal. Those tubes small enough to enter the guinea pig meatus have an internal diameter so small that a considerable degree of protection is afforded by the tubing itself. (See Table II.)

In order to use such an arrangement successfully, it is essential that either the apparatus be so fastened to the animal that it will follow all the movements it may make without becoming loosened, or that the head of the animal be immobilized. The latter procedure seemed preferable and as I knew of no apparatus suitable for this purpose a new one had to be made. It consists of a base of wood 10 cm. wide by 4 cm. thick by 35 cm. long, on which two strips of canvas 6 cm. wide are tacked. These strips run across the base and at either end serve as hinges to which are attached the side pieces, each of which is made of thin narrow strips of wood nailed together to form a latticework 23 cm. long by 8 cm. wide. When closed, the base and side pieces form a space with a triangular cross section 4 cm. wide at the base and nearly 8 cm. high; the spaces of the lat-

ticework permit parts of the body of an animal to bulge. To further immobilize the head, on either side an obliquely placed bar of wood was attached to the inner side of the lower strip of the latticework near one end. These fit behind and under the angle of the jaw, and, being movable, can be adjusted readily to the size of the animal. To prevent vertical movement of the front of the head, a completely removable crossbar of wood is fastened under the front part of the lower jaw; this is also adjustable by means of notches in the latticework. When properly adjusted, the ears of a guinea pig being held are well exposed between strips of the side pieces. The apparatus of the dimensions given is adaptable to guinea pigs ranging from 200 to 400 grams. Experience has shown that when one sets the "jaw pieces" of this holding apparatus tight enough to completely immobilize the head of an animal the external auditory canal is liable to be partly or even totally pinched shut. When set loose enough to assure an open canal a slight amount of movement is possible; it was found that most animals did not try to move after the first struggles while fastening them in. A few animals moved after packing of the wax and required repacking; only one animal out of some fifty used persisted in moving so much that it was impossible to satisfactorily place a packing. In every case, in order to check up on the loosening of the packing and a possible entry of the detonation wave thereby, the wax was examined carefully after the shooting, and the condition of it has been made a matter of record in the tabulated results.

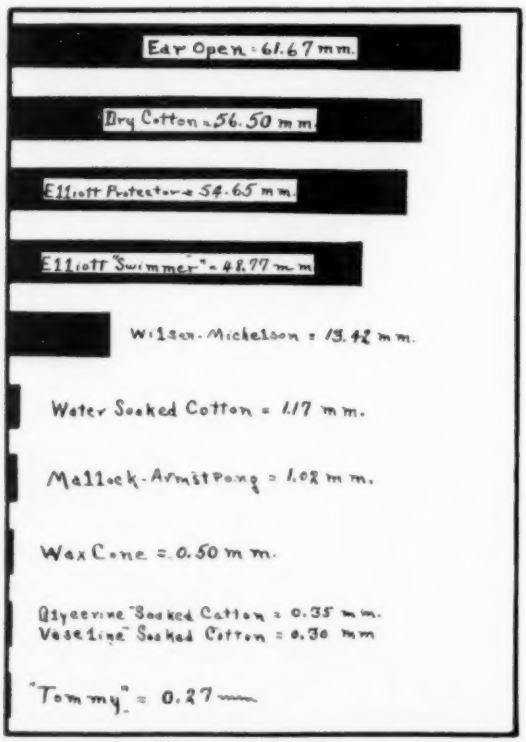
The source of the detonation wave used was the firing of a 45 caliber Colt automatic pistol, using Peters' ammunition. The experiments were conducted in the open at a place where a hillside forms a suitable stop for bullets. While the detonation is not of the initial intensity of that caused by an exploding shell or by the firing of a large artillery piece, yet by using the relatively small detonation at a short distance the force is doubtless approximated to that in the zone about a larger explosion in which ears are injured without causing death by "shell shock." A series of controls showed 15 cm. to be a suitable distance, the tympanic membrane being regularly ruptured with coagulated blood and edema present in the mucous membrane at autopsy.

Submitting animals to large gun and shell detonations might be done at some of the munitions proving grounds and at certain government works, if proper authority and some laboratory facilities were provided, and such tests would be an interesting check on these.

The routine procedure for each experiment was as follows: (1) The hair projecting over the ear to be protected (the left ear was used in all cases) was trimmed with scissors; (2) the animal was fastened in the holding apparatus and the apparatus adjusted so as to be sure the external auditory canal was not pinched shut; (3) the animal in the apparatus was then turned on one side and the glass tube, with the large end already inserted in the rubber ear in which the protecting device to be tested had been carefully adjusted, was placed over the meatus (or inserted in it in the case of the small tubes used a few times) and the soft wax mixture carefully packed as already described above; (4) a cord passed through the rim of the rubber ear was fastened to the framework of the apparatus in such a way as to support the weight of the ear and prevent it from

becoming loosened by gravity when the animal and apparatus are placed upright again; (5) the apparatus and contained animal were placed on the ground selected, the muzzle of the gun held at the predetermined point giving the desired distance and direction and the shot fired; (6) the condition of the wax packing was noted immediately and the animal released as soon as possible.

The damage to the ear by detonations has been discussed fully in the previous article. The variations from normal that indicate injury to the hearing are to be sought for in two places in animals, (1) the middle ear parts and (2) the cochlear parts. Clinical tests on the hearing ability of animals are very unsatisfactory when a total loss of hearing has not occurred, and that even this is dif-


Ear Open = 61.67 m m.
Dry Cotton = 56.50 m m.
Elliott Protector = 54.65 m m.
Elliott "Swimmer" = 48.77 m m.
Wilson-Michelson = 13.42 m m.
Water Soaked Cotton = 1.17 m m.
Mallock-Armistrong = 1.02 m m.
Wax Cone = 0.50 m m.
Glycerine Soaked Cotton = 0.35 m m.
Vaseline Soaked Cotton = 0.30 m m
"Tommy" = 0.27 mm

A graphic presentation of the results with the 44 caliber revolver.

ficult to determine is evidenced by the heated discussion from 1892 to 1895 as to whether animals with the eighth cranial nerve severed some time previously could hear. The experienced laboratory worker, W. Wundt, was deceived, among others; with such a record of the interpretation of hearing tests, I am depending entirely upon organic injuries to judge the damage done to the hearing. The condition of the middle ear parts may be observed with the unaided eye at autopsy; the condition of the cochlear parts can be told only by microscopic examination preceded by careful histologic preparation. Yoshii has stated that the maximum degree of change in the cochlear parts is reached on the second to third day after the injurious detonation. He used only animals exposed to the

full force of a detonation. For this reason I killed the animals used about forty-eight hours after exposure.

In a series of experiments conducted during the past two years I have been trying to find the best technic for handling cochleæ, and have tried most of the procedures recommended by those who have reported work on cochleæ and also some new variations. This work was done preliminary to experiments on the physiology of hearing, which the war has postponed indefinitely, but which I hope at some future time to carry out. At that time the results of the various technical procedures will be fully considered. For the present it suffices to say that in these experiments I am using the method which has given me the best general results. It will be given in full in the report of the condition of the cochleæ of these animals submitted to detonations. As the method includes fixation of the tissue by vascular injection with a preliminary thorough washing out of the blood by physiologic saline solution, inflammatory changes in the middle ear could not be judged by the coloration at autopsy, but had to be judged only by the presence of coagulate and edema. The significance of the loosening of the mucous membrane was not recognized by me in the first animals used and accordingly it was only occasionally recorded at first. It was not until a group of control animals that had not been exposed to detonations was examined that I became certain that the loosening of the mucous membrane was not an artefact due to the injection procedure. This accounts for the blanks in the records of some of the animals with regard to the presence of edema. The condition of the tympanic membrane is not affected by the injection and may be directly observed, as may also the presence of areas of coagulate which are not removed by the washing out procedure.

REASON FOR DIVIDING THE REPORT

Since the handling of the cochleæ by the method used, preparatory to sectioning, requires at the very least 85 days, and the first animals were used September 5, it has seemed advisable to report the observations on the middle ear parts without waiting for those on the cochlear parts, especially since the results are positive, certain devices having protected the middle ear parts better than others, and since the injury to ears of soldiers is occurring every day. The study of the sections of the cochleæ, when prepared properly, should give more evidence, but its nature can not be predicted. It may show marked differences between degree of protection afforded by those devices which best protected the middle ear parts. Due to the time required for sectioning, staining, and studying them, and teaching duties, it will probably be late next spring before I can report the cochlear condition.

OBSERVATIONS ON THE MIDDLE EAR PARTS

The observations are presented in tabulated form; the tables showing the control experiments being placed before those of the preventive measures tested. The items shown in the tables need no other explanation than that already given above.

The finding of normal middle ear parts in one side of No. 17 and No. 18,

TABLE I

CONTROL EXPERIMENTS

ANIMALS WITH BOTH EARS OPEN; NO APPARATUS IN EITHER EAR

GUINEA PIG NO.	DISTANCE OF NEAREST EAR FROM MUZZLE	NO. OF SHOTS FIRED	SIDE	CONDITION OF TYMPANIC MEMBRANE AT AUTOPSY	AMOUNT OF COAGULATE IN AND ON MUCOUS MEMBRANE OF THE MIDDLE EAR	EVIDENCE INDICATING EDEMA OF THE MUCOUS MEMBRANE	REMARKS ESPECIALLY ON THE POSITION OF THE PISTOL
45	60 cm.	1	Right	Intact — radial streak of coagulate	Small	Slightly loosened	Shooting from above and in front of animal downward at 20° angle with the horizontal
			Left	Intact	One large area	Slightly loosened	
44	30 cm.	1	Right	About ⅓ of area broken	Medium	Loosened	Shooting from above and in front downward about 20° slightly along left side
			Left	Whole center gone	Small	Loosened	
16	15 cm.	1	Right	Off along most of circumference	Medium		From above and behind directly over animal
			Left	Not quite as bad as right side	Medium	Loosened	
17	15 cm.	5	Right	Intact	None	None	(See text matter below) From above and in front along right side of animal
			Left	Completely gone	Large		
18	5 cm.	3	Right	Intact	None	None	(See text matter below) From above and in front along left side
			Left	Completely gone	Large		
39	10 cm.	2	Right	Off of ¾ of circumference	Medium	Loosened	Shooting from directly above
			Left	Fringes only left	Large	Loosened	

after shots fired at so short a distance, is to be interpreted only on the basis of the external canal having been pinched shut by the jaw pieces of the holding apparatus. These cases were among the first animals used and thereafter special precaution was taken to prevent repetition of this condition, as has been mentioned in the description of the routine procedure. For a short time after the shooting, the animals appeared to be somewhat dazed, but none were unconscious when released. The last one listed above was not placed in the holding apparatus and it was able to run away after each shot; it did not stagger, but seemed somewhat dazed.

The controls on the possible protection afforded by the apparatus used to hold the preventive devices show clearly that there is an approximately equal damage to the middle ear parts with and without the rubber "ear" and glass tube in place, when using tubes 2.5 mm., and upwards, in internal diameter at the smallest part. With the 2 mm. tube, a certain degree of protection may be

TABLE II

CONTROL EXPERIMENTS

ANIMALS WITH GLASS TUBE AND RUBBER "EAR" (WITHOUT ANY PREVENTIVE DEVICE INSERTED) IN ONE EAR AND THE OTHER EAR OPEN

GUINEA PIG NO.	SIDE	SMALLEST DIAMETER OF THE GLASS TUBE IN MM.	CONDITION OF WAX PACKING AFTER SHOOTING	CONDITION OF TYMPANIC MEMBRANE AT AUTOPSY	AMOUNT OF COAGULATE IN AND ON MUCOUS MEMBRANE OF THE MIDDLE EAR	EVIDENCE INDICATING EDEMA OF THE MUCOUS MEMBRANE	REMARKS ESPECIALLY ON THE POSITION OF THE PISTOL
19	Right	3.5	O.K.	Ruptured badly	Medium		Two shots — one at 10 cm. from each ear backward along sides
	Left			Ruptured badly	Medium		
52	Right			Off on ¾ of circumference	Large	Slightly loosened	Usual arrangement*
	Left	3.5	O.K.	Fringe	Large	Badly loosened	
51	Right			Fringe	Large	Slightly loosened	Usual arrangement*
	Left	3.1	O.K.	Fringe	Large	Slightly loosened	
50	Right			Fringe	Large	Loosened	Usual arrangement*
	Left	2.5	O.K.	Fringe	Large	Loosened	
49	Right			Off on ⅓ of circumference	Medium	Loosened	Usual arrangement*
	Left	2.0	O.K.	Off on ½ of circumference	Medium	Badly loosened	
47	Right			Off on ⅘ of circumference	Medium	Loosened	Usual arrangement*
	Left	2.0	End of glass partly stopped	Intact	Streak about tympanic ring	None	
42	Right			Fringe	Medium	None	Usual arrangement*
	Left	2.0	End of glass partly stopped	Intact	Small	None	
43	Right			Fringe	Medium	Slightly loosened	Usual arrangement*
	Left	1.5	O.K.	Intact	None	None	

*One shot at 15 cm. fired with the muzzle of the pistol in front of and slightly above the animal, and pointing downward along the left side at an angle of about 20° with the horizontal, just avoiding the holding apparatus with the bullet.

afforded, but I am more inclined to attribute the results obtained with this tube to the fact of its being too short to fit properly into place, thus permitting wax to pass beneath it in packing. As will be observed in Table IV, the larger tubes were used for the most part, and the results obtained with the 2 mm. tube have been discounted in considering the effectiveness of any device with which it was used on part of the animals.

Table III has been inserted in order to show the regularity with which the detonation and arrangement used caused severe injuries to the middle ear parts of

TABLE III

RECORD OF THE UNPROTECTED EAR (CONTROL EAR) OF THE ANIMALS WITH WHICH THE OTHER EAR WAS "PROTECTED"*

GUINEA PIG NO.	CONDITION OF TYMPANIC MEMBRANE AT AUTOPSY	AMOUNT OF COAGULATE IN AND ON MUCOUS MEMBRANE OF THE MIDDLE EAR	EVIDENCE INDICATING EDEMA OF THE MUCOUS MEMBRANE
21	Off on ½ circumference	Medium	
22	" " ¾ "	Small	
23	" " ⅘ "	Small	Loosened
24	" " ⅛ "	Large	
25	" " ½ "	Large	Loosened
26	" " ½ "	Medium	
27	" " ½ "	Medium	
28	Only fringes left	Medium	
29	¼ area gone	Very small	
30	½ area gone	Small	
31	Only fringes left	Large	
32	" " "	Large	
33	" " "	Small	
34	" " "	Large	Loosened
35	" " "	Small	None
36	Off on ½ circumference	Large	Loosened
37	A radial slit	Only on edges of slit—no other	Loosened
38	Only fringes left	Large	Loosened
40	Whole center out	Large	Loosened
41	Off on ¾ circumference	Large	None
53	Only fringes left	Medium	Slightly loosened
54	Whole center out	Medium	Slightly loosened
55	⅔ area out	Medium	Slightly loosened
56	A wide fringe left	Large	None
57	Only a fringe	Very large	Badly loosened
58	" " "	Medium	Slightly loosened
59	" " "	Medium	Badly loosened
60	" " "	Medium	Badly loosened
61	Completely gone	Small	Slightly loosened

*The right ear was open in all cases. For the shooting arrangement, see footnote to Table II.

the unprotected ear of the animals which had the other ear "protected." It should be recalled in studying the following tables that the gun was so placed that the protected ear received a heavier wave than the unprotected one.

DISCUSSION

The above tabulated observations indicate the order of efficiency of the devices in reducing the intensity of the detonation wave. In discussing them I wish to add to these observations certain other factors which must be considered in selecting for military use. At this point it is well to recall that the cochleæ, when sectioned and studied, may give evidence indicating a change in this order, and very probably will help to subdivide the groups.

In the first group I would place the "Tommy" and the Mallock-Armstrong devices. Both protected the middle ears of the guinea pigs equally well. Of the two, for use in any but military life I would prefer the Mallock-Armstrong, for two reasons. In the first place, ordinary sounds are heard somewhat better; and, in the second place, if one is fitted with the proper size, the solid end of the device does not cause the irritation while wearing that the continual pressure of

TABLE IV

RECORD OF THE "PROTECTED" EARS*

PREVENTIVE DEVICE BEING TESTED	GUINEA PIG NO.	SMALLEST DIAMETER OF THE GLASS TUBE IN MM.	CONDITION OF WAX PACKING AFTER SHOOTING	CONDITION OF TYMPANIC MEMBRANE AT AUTOPSY	AMOUNT OF COAGULATE IN AND ON MUCOUS MEMBRANE OF THE MIDDLE EAR	EVIDENCE INDICATING EDEMA OF THE MUCOUS MEMBRANE
Scientific Ear Drum Protector "Tommy"	26	2.5	O.K.	Intact	None	
	56	3.5	O.K.	Intact	None	None
	32	2.5	?	Intact	None	None
	25	2.5	Bit of wax in tube	Intact	One area	
Mallock-Armstrong Ear Defender	21	2.5	O.K.	Intact	Two areas	
	53	3.5	O.K.	Intact	None	None
	22	2.5	Loosened	Intact	None	
Wax Cone of the Italian Navy type	33	3.5	O.K.	Intact	None	None
	34	3.5	O.K.	Intact	Very small	None
	57	3.5	O.K.	Intact	Slight	None
Cotton saturated with vaseline well worked in	60	3.5	O.K.	Intact	None	None
	61	3.5	O.K.	Intact—radial streak coagulate	Along ¼ tympanic ring	Very slightly loosened
	40	2.0[1]	O.K.	Intact	None	None
	41	2.0[1]	Slightly loosened	Intact	None	None
Cotton saturated with glycerin—air was worked out as much as possible[2]	55	3.5	O.K.	Intact	Streak about tympanic ring. Two other areas	Slightly loosened
	59	3.5	O.K.	Intact	¾ of circumference tympanic ring	None
	37	2.0[1]	O.K.	Intact	None	None
Dry cotton packed firmly	35	3.5	O.K.	Intact—Clot on outer surface	One area	Loosened
	58	3.5	O.K.	Radial slit	Edges of slit—medium elsewhere	Badly loosened
	36	2.0[1]	O.K.	Intact	Along ⅛ tympanic ring. One other large area	
Elliott Perfect Ear Protector[3]	23	2.5	O.K.	Off on ⅖ circumference	None	Loosened
	28	3.5	O.K.	Intact	Along ½ tympanic ring	
	54	3.5	O.K.	Intact	Along all tympanic ring	Slightly loosened

TABLE IV (CONT'D)

RECORD OF THE "PROTECTED" EARS *

PREVENTIVE DEVICE BEING TESTED	GUINEA PIG NO.	SMALLEST DIAMETER OF THE GLASS TUBE IN MM.	CONDITION OF WAX PACKING AFTER SHOOTING	CONDITION OF TYMPANIC MEMBRANE AT AUTOPSY	AMOUNT OF COAGULATE IN AND ON MUCOUS MEMBRANE OF THE MIDDLE EAR	EVIDENCE INDICATING EDEMA OF THE MUCOUS MEMBRANE
Device submitted to the Council by Dr. J. G. Wilson and Prof. A. Michelson	27	2.5	O.K.	Intact	Along ⅔ ring. Other small areas	
	30	3.5	O.K.	Intact	3 streaks along parts of ring. Several small areas	
	31	3.5	O.K.	Hole about 3 mm. in diameter	Several small areas one large	

*The left ear in each case; for the shooting arrangement, see the footnote to Table II.
[1]Controls indicate that the 2 mm. tube is too small, so the results with it must be discounted.
[2]A fourth animal was found at autopsy to have a thickened tympanic membrane due to an old infection, and so has not been included.
[3]Two more animals were tried with this device; with both the wax packing was not in good condition when examined after the shooting, and accordingly the results are not included. Both showed positive injuries.

the elastic rubber bulb of the "Tommy" does. But there is one serious objection to the Mallock-Armstrong device for army use. It has already been given in discussing the Wilson-Michelson instrument, but is so important that I will repeat it. A projectile passing alongside the head, wounding only the pinna or the outer part of the external meatus, in itself a relatively slight wound and of quite common occurrence, would shatter any hard obturator present and form secondary projectiles of the fragments, causing a much more severe wound. A further objection to the Mallock-Armstrong instrument is the difficulty in keeping dirt and mud from clogging the gauzes and membrane. There is nothing simpler to keep clean than a "Tommy" and for army use it seems to me the best of those tested.

The wax cone of the Italian Navy type comes next in order, followed closely by cotton soaked with vaseline. Because of the universal availability of cotton and vaseline I consider the degree of protection afforded by it worthy of note by those to whom the first named two mechanical devices are not accessible. The extra protection afforded by mixing the cotton with vaseline is well worth the trouble, as a comparison of this record with that of dry cotton shows.

Cotton soaked with glycerine did not protect quite so well as that saturated with vaseline; the explanation probably lies in the greater viscosity of the vaseline.

The results with dry cotton are particularly interesting in view of the unsatisfactory experience that various armies and navies have had with it in actual use. Since this was given in my previous article, it will not be repeated here. While only three animals were used, the consistency of the failure to protect is a beau-

tiful confirmation of the military experience with it. Doubtless the correct explanation is the fact of its being air-containing, as several men have urged. Cotton soaked with water was not tested; I will try it if I have occasion to run a further series with new mechanical devices. On theoretical grounds, water-soaked cotton should give protection comparable to that soaked with glycerine.

The Elliott Perfect Ear Protector and the Wilson-Michelson device rank together with dry cotton as having given the least protection to the middle ear parts of the animals used. With all three preventive measures every animal showed positive injuries, and one out of each group of three animals had a ruptured tympanic membrane.

Testing of the devices for the relative amount to which they reduce ordinary sounds has given rather contradictory results so far, due probably to the crude nature of the methods employed and doubtless in part to the individuals acting as subjects having placed the devices more or less poorly in their own ears; but this latter is a thing that will occur in the actual use of them. So I know the degree to which each excludes ordinary sounds only in a general way as yet; but I feel safe in saying that all the devices permit conversational sounds to be readily understood; loud sounds, such as commands and signal whistles, catch the attention at a considerable distance. Of the mechanical devices, the Elliott reduces ordinary sounds the least and the "Tommy" the most, the "Tommy" cutting it down more than dry cotton does, but all of the mechanical devices permit more to pass than do the wax or the soaked cotton plugs.

PROJECTED EXPERIMENTS

A further series of experiments is projected and will be carried out as rapidly as the time available from teaching duties will permit; it is hoped to have these completed before the cochleæ of the present series are ready to begin sectioning. Again using the rubber ear as a means of holding the preventive devices, the glass tube will be led to a tambour and the record be made on smoked paper instead of in the ear of an animal. These records are intended as a check on the relative efficiency indicated by the reaction on the guinea pigs, but could not take the place of these animal experiments, for the amount of shock necessary to cause injury will not be shown; merely the relative amount of detonation waves that pass the preventive devices. I hope by this same method, using a very delicate tambour, to obtain data on the relative amount which the various devices reduce the intensity of ordinary sounds.

ACKNOWLEDGMENTS

I wish to express my thanks here to Dr. Whitman for his advice on the rubber ears, and to Mr. G. C. Lubke for his careful work making the same, and to Mr. Frank O. Novy, medical student, for aid in conducting some of the experiments.

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LABORATORY METHODS

A COMPACT BOX FOR THE COLLECTION AND TRANSPORTATION OF BLOOD FOR HEMOGLOBIN ESTIMATIONS AND CELL COUNTS*

By Stanley P. Reimann, M.D., and Edward P. Heller, M.D.,
Philadelphia, Pa.

THE following is a description of the box which has given much satisfaction in daily hard use in the Lankenau Hospital for several months. Bills for new blood pipettes and hemoglobinometers have fallen to zero since its introduction, while its compactness and completeness have saved much time. It is designed to accommodate nine complete counts which are collected on the wards, where the hemoglobin estimation is made immediately, and the filled pipettes are then transported to the central laboratory for counting.

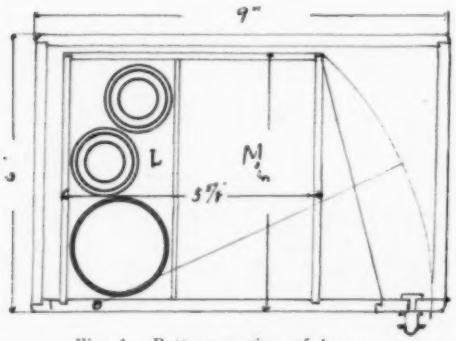

Fig. 1.—Bottom section of box.

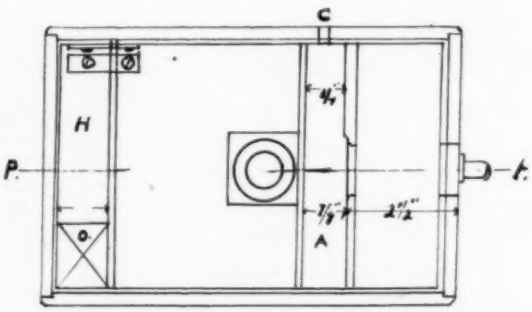

Fig. 2.—Upper compartment. *A*, space for hemoglobinometer; *H*, battery; *O*, block to hold battery in place.

The outside dimensions are 11 by 9 by 5½ inches. There is an upper compartment 8 by 4½ by 4¼ inches with a hinged lid to accommodate a Dare hemoglobinometer and cut to allow the eyepiece to project through the side of the compartment. The milled head which controls the color disc protrudes through the top of the lid, and can be moved from without, while another slot cut in the back of the compartment brings the scale into view. A small electric bulb and connections are fastened in the proper position in front of the blood and color disc; the battery is in a compartment to the side and the current is controlled by a small switch on the outside of the box immediately under the projecting eyepiece. A small piece is sawed from the top of the hard rubber movable portion of the Dare to make room for the lid to close. Ample space is left to provide small compartments for blood lancet, rubber tubing, alcohol-soaked cotton, bottles of acetic acid and saline, and bundles of horsehair and capillary

*From the Department of Pathology of the Lankenau Hospital, Philadelphia, Pa.

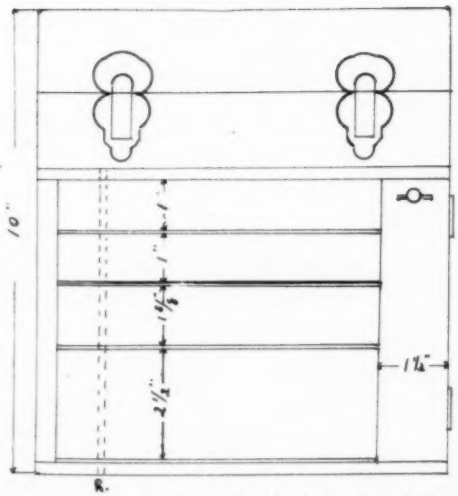

Fig. 3.—Front of box, showing four drawers and the upright which locks the drawers. The clamps for the lid are Corbin bag clamps.

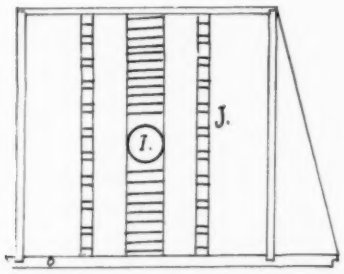

Fig. 4.—Shows a drawer for holding blood pipettes. *J*, coil spring; *I*, notched strip.

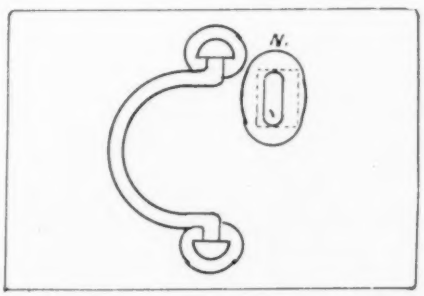

Fig. 5.—Top of box. *N*, opening through which the milled head of the hemoglobinometer protrudes; covered by a bulged lock escutcheon.

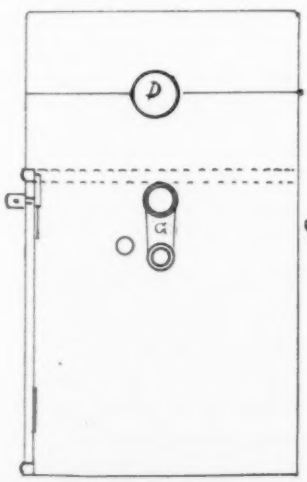

Fig. 6.—Side of box. *D*, hemoglobinometer eyepiece; *G*, switch.

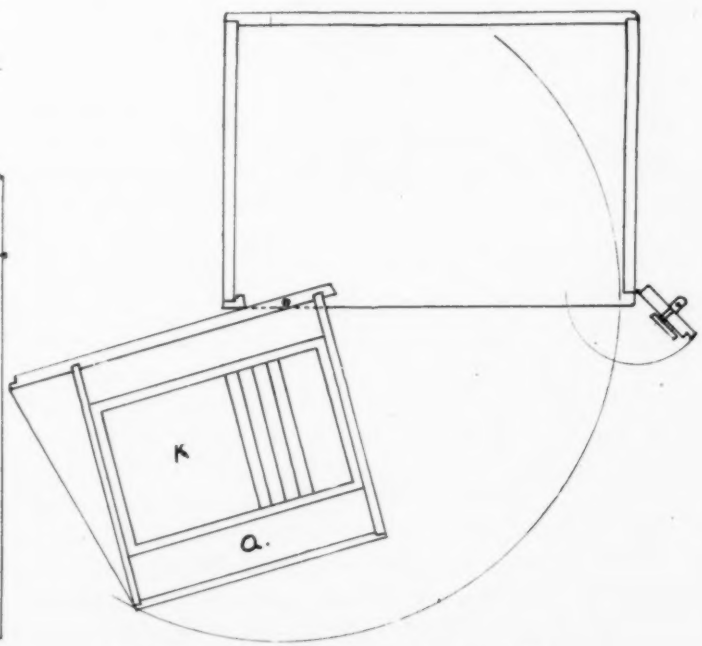

Fig. 7.—*A*, drawer open; *O*, space for hemoglobin glass slips; *K*, box for slides.

tubing for coagulation time estimations. The inside of the lid is painted a dull black. Comparisons of hemoglobin readings using candle light as provided for in the Dare, and the small electric light in the box have shown practically no differences.

The lower compartment, which is 8 by 6 by 4¾ inches, inside dimensions, contains four drawers pivoted, which swing out independently or together, and are locked closed by an extension of their bottoms which are held in place by a thin hinged strip on the side of the box, and this is locked by a small turn key. In the upper drawer are small squares of gauze and cover slips. Slots are provided in the second and third drawers to hold red and white cell pipettes, and these are further steadied by a spring passing across the middle of the drawer between the turns of which the pipettes are placed. An ordinary slide box is

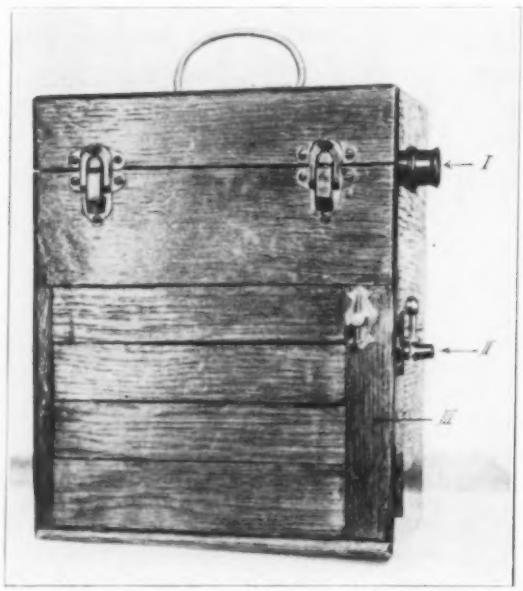

Fig. 8.—Blood box closed for transportation. *I*, eyepiece; *II*, electric switch; *III*, upright for locking drawers.

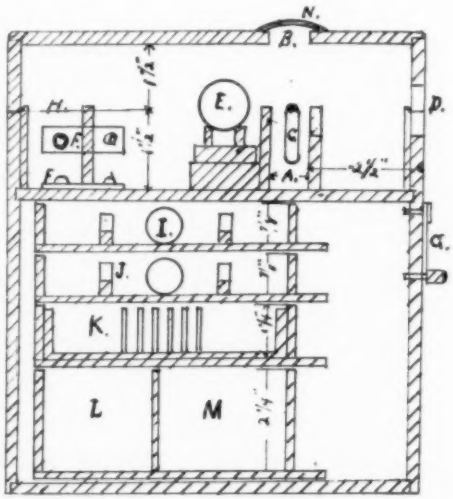

Fig. 9.—Section cut at *P*, Fig. 2. *A*, body of Dare hemoglobinometer; *B*, hole in lid for milled head of Dare; *C*, hole in back of box through which the scale can be read; *D*, hole in side of box for eyepiece; *E*, electric lamp; *F,F*, plates of brass with screw heads to form a circuit through lamp and switch; *H*, space for battery; *G*, switch, *I, J, K, L, M*, drawers to hold pipettes, glass slides, gauze, etc.

glued into the fourth drawer to hold blood smears. If they are made on cover slips, a space can be provided in the box. On either side is room for the hemoglobin glass slips and holders. The inside dimensions of the drawers are 5½ by 4½ by 1 inches. A handle on the lid provides for carrying. When filled with pipettes, etc., it weighs 10 pounds. The accompanying photographs, for which we are indebted to Dr. A. G. Miller, of the Department of Roentgenology, will show the main features.

Our thanks are expressed to Mr. E. C. Lovejoy, the house carpenter, not only for the actual workmanship, but also for many details of construction.

AIDS TO LABORATORY EFFICIENCY

By Miles J. Breuer, M.A., M.D., Lincoln, Neb.

THERE is a constantly growing number of practitioners in the medical profession who realize that clinical observation ought to be supported by laboratory study. Many of these, in fact most of those who are located in smaller towns, are men who can not afford to pay a laboratory technician's salary, and who, at the same time, are too busy with their patients to spend very much time in the laboratory themselves. Even the simplest routine tests, to be of value, must be done carefully, and require time; and a man with a waiting-room full of people hardly has the patience to go through a Widal test or a gastric analysis with the same elaborateness that the internes use in a hospital laboratory.

I have always been of the opinion that even the busiest practitioner can do a considerable volume of his own laboratory work if he is so inclined, by spending a few spare hours in arranging the laboratory and apparatus so that they are convenient and efficient. By putting in a little time when he is not pressed with work, he can so arrange things that when he does have to ask a patient to wait while a test is performed, he can run through the latter with a minimum expenditure of time and energy. The main essential is to eliminate unessential motions and operations, and it is surprising how much one's time in the laboratory can be cut down, by attention to a few simple things. Especially since it is now possible to purchase reagents, media, and stains ready made-up or nearly so, is it desirable for every physician to do as much of his own laboratory work as possible, in preference to not having it done at all.

Below are described a number of methods and pieces of apparatus which have enabled me to do a great deal of clinical laboratory work, although I have only a limited amount of time to spend in the laboratory. Some of the ideas are original, some are not; the sources of the latter are mostly forgotten and not recorded. Naturally, these things will be of interest rather to the practitioner than to the man who is at home in the laboratory.

In order to run through a test with rapidity and certainty, it is necessary to have it well in mind. The next best thing, when this is not practicable, is to have a card index of the tests in common use. The preparation of such an index is not as much of a task as might at first thought seem, for when the test is being studied over for the first time while learning to do it, it takes but little additional time to outline or abstract it on a card. Later when the work is being done, it is only necessary to take the card from its box, which should be kept in the laboratory, and keep it in front of oneself while working.

Take the matter of making a Gram stain, or a stain for tubercle bacilli; the average physician is apt to consider the procedure rather tedious; and it is tedious, if he takes the slide in a pair of forceps, holds it over an open flame, and drops the stain on it out of a bottle each time. For the tubercle method I have provided an iron plate, which I heat over a Bunsen burner, hot enough to make a drop of water sizzle; on this I lay the slide, removing the burner, and

covering the slide with carbol-fuchsin, leaving it there for five minutes, during which time I can be attending to something else. For the rest of the process, and for the Gram stain and other special stains, I use Coplin jars filled with the stain. For destaining, I have Coplin jars filled with the necessary alcohol. With these, staining is merely a matter of transferring the slide from one jar to another, and while it is in the jar, other work can be attended to. In case of most of the stains, it makes little difference if the slide is left in the stain longer than the time prescribed in the textbook. In place of the Coplin jars, ordinary wide-mouthed bottles, deep enough to cover a slide, may be used.

Reaching up on a shelf, taking down a bottle, removing the stopper, and pouring out the reagent, consumes an appreciable amount of time, which be-

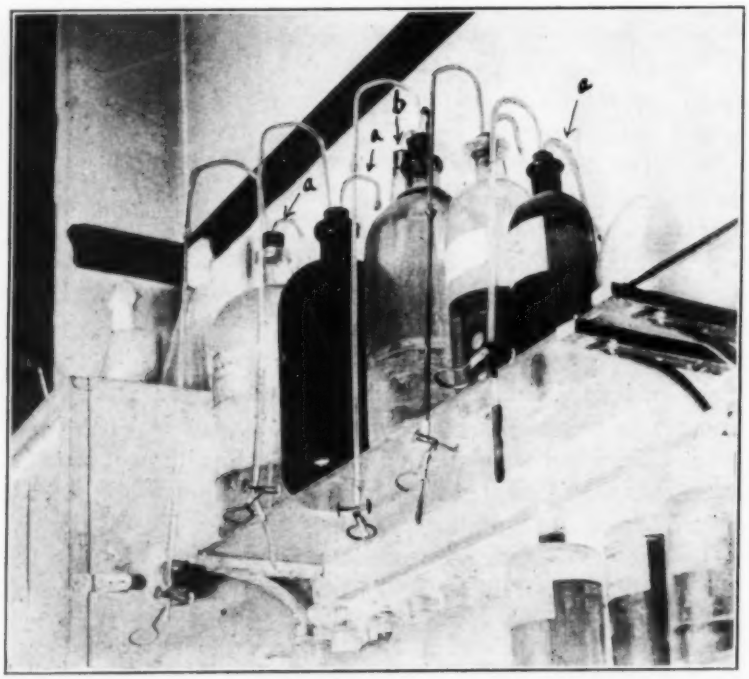

Fig. 1.—Siphon bottles.

comes considerable when frequently repeated. The installation of siphon delivery bottles for the more common reagents so that merely the pressure on a pinchcock suffices to release the flow, is easy and needs no further explanation than the illustration (Fig. 1). At *a* is a tube plugged with cotton, to allow ingress of air to replace the liquid that runs out. I use this method for handling the following: distilled water and physiologic salt solution, both kept sterile; N/10 sodium hydroxide, which is protected by a wash bottle containing caustic soda sticks *b*, to remove the carbon dioxide from the entering air and avoid weakening the solution; Benedict's solution, and alcohol. Tenth-normal sodium hydroxide and hydrochloric acid are also kept in burettes fastened to the wall, ready for instant use. The top of the burette should be stoppered with a rubber

stopper, which is removed when the burette is used. The sodium hydroxide burette should have a rubber delivery tube and pinchcock instead of a glass stopcock, as the alkali causes the glass to stick. It would be desirable to keep nitric acid in such a siphon delivery bottle, as it is very frequently used, but

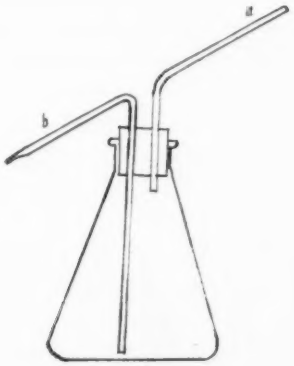

Fig. 2.—Wash bottle.

it is a little too energetic to be handled this way, as there is danger of its being scattered about.

Another point in the handling of reagents, is the use of wash bottles for distilled water, physiologic salt solution, and alcohol. Very frequently during the

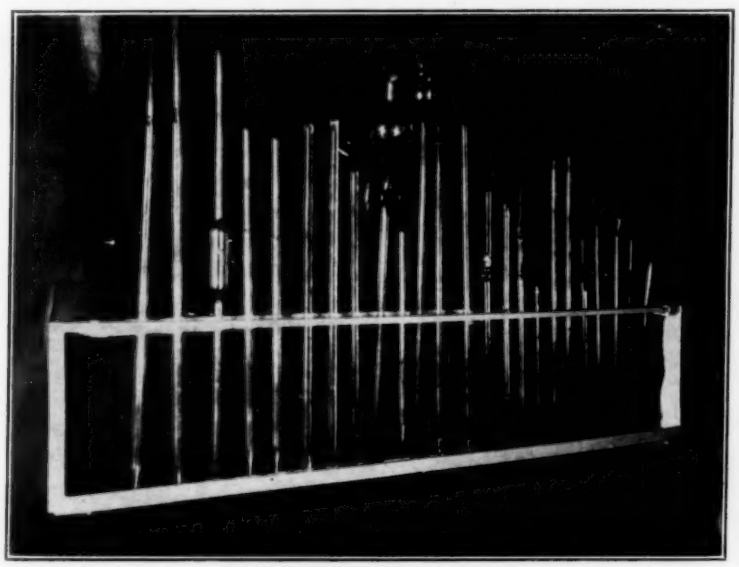

Fig. 3.—Pipette rack.

course of tests it is necessary to use small amounts of these substances. If they are kept in wash bottles of the form shown in Fig. 2, blowing into tube *a* will deliver a small quantity, or inclining the bottle so that the fluid runs out of *a* will deliver a larger quantity.

In most laboratories that I have seen, pipettes, glass rods, platinum needles and loops are kept in a drawer; when one is needed, it is necessary to open the drawer and rake among its contents to find what is wanted. I have adopted the pipette rack shown in Fig. 3, made of thin pieces of wood fastened to the wall over the work table; this keeps all the rods and pipettes in plain sight and instantly available. It consists of an upper strip with holes through which the pipettes are placed, and a lower strip with hemispherical depressions made with a twist drill. At the bottom of each of the latter is a small hole entirely through the wood, to drain out the water, when pipettes are placed wet in the rack.

It is possible to save much lost motion by attention to small matters about the use of a microscope. The light is important. I never use daylight, but have

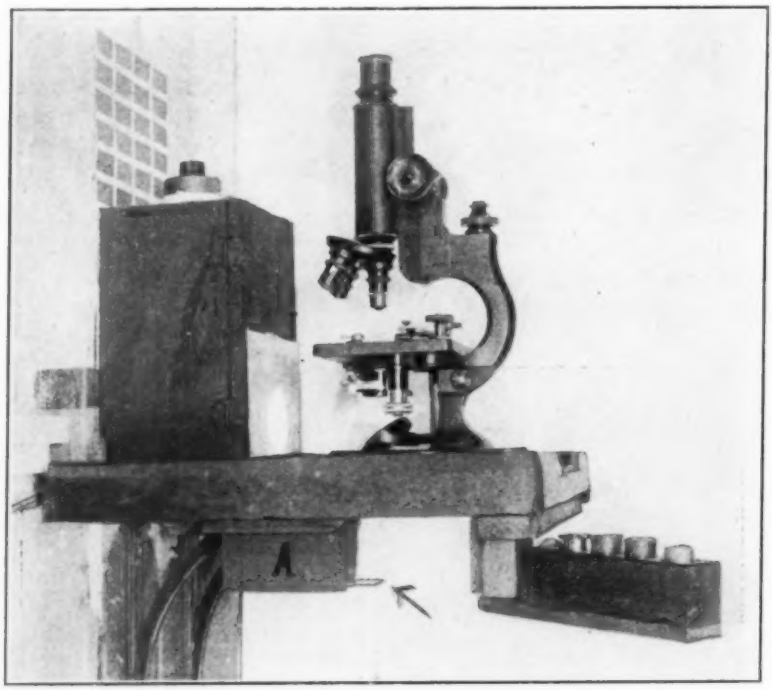

Fig. 4.—Microscopic shelf.

a 100-watt nitrogen Mazda lamp and a blue filter, which will give correct color rendering. This gives a constant standard illumination for comparison, and is instantly available, day or night, with no other arranging or manipulation than the mere turning of a switch. Many laboratories have the light under the table, coming up through the base of the microscope, whose mirror is swung out of the way. This method is good if it is possible to interpose a convex lens of proper focal length; otherwise definition suffers. The condenser of the microscope is made to handle parallel rays. If the light comes from a source closer than four feet away, it is necessary to use some method of rendering the rays parallel; otherwise the best results can not be obtained.

I have a special shelf fastened to the wall for microscopic work. The

various extra oculars, and bottle of immersion oil, that come set in a block in the microscope box, were pivoted with their block on the under side of the shelf, so that they can be swung out when needed. An arrangement has also been provided which always keeps a clean slide within easy reach. This is shown at *A* in Fig. 4, with an arrow pointing to a partially delivered slide. Fig. 5 shows the details of construction. In Fig. 4, above the box containing the light, is shown a chart of brightly-colored squares for the purpose of resting the eyes when fatigued by prolonged microscopic examination.

The cleaning of hanging-drop slides is a tedious operation for the busy man, especially when they are contaminated with pathogenic organisms. Much time can be saved by the arrangement illustrated in Fig. 6. A cylinder is used, made from a short section of half-inch glass tubing, ground flat on both ends by an optician. The shorter the section of the tubing, the better the definition obtainable, as the drop is then closer to the focus of the rays from the condenser. The cover-glass with the hanging drop is set on the cylinder as shown, and nothing becomes soiled or contaminated except the cover-glass, which can be taken

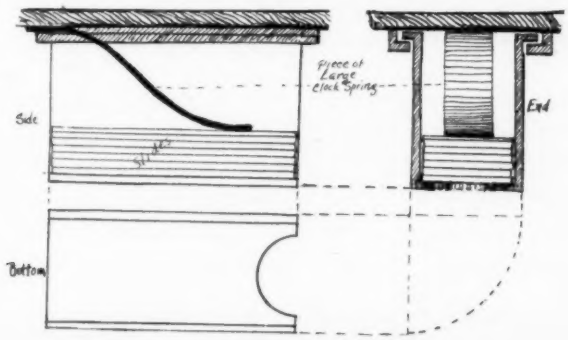

Fig. 5.—Container for slides.

off after the examination is over, and dropped into a jar of sulphuric acid and potassium dichromate mixture, which is always kept standing in the laboratory to receive slides and other small pieces of apparatus requiring cleaning. By using such cylinders, two or three hanging drops may be kept together on the same slide, which is desirable, for instance, when the agglutination tests for typhoid and the two paratyphoids are being done.

An ordinary suction pump, operated by water pressure, such as is screwed to the water faucet, is a great time saver about the laboratory. Pressure tubing (such as is used on stethoscopes) is used for the connections, and a large bottle is interposed in the suction tube by means of two bent glass tubes in a rubber stopper; the purpose of this is to catch fluids that are being aspirated, as their passage through the pump will interfere with its action. This pump can be used, for instance, for cleaning blood counting pipettes. The pipette is slipped into the connecting tube, and dipped for a moment into water, alcohol, and ether, the suction drawing through enough of the fluid to clean the pipette, and the entire operation not requiring over one minute. Pipettes for serum work, and small measuring pipettes can be cleaned in the same manner. For separat-

ing serum from corpuscles, and separating other liquids, decanting, and to replace siphonage, this apparatus saves much time and work. When it is desired to keep the separated fluid, a small wash bottle can be interposed on the connection to catch it. For aeration methods, the pump is indispensable. I have made this pump do duty in gastric aspiration, and in the office operating room in mouth work, to get rid of saliva.

Fig. 7 illustrates a form of pipette that I have found very convenient for serum work and work with vaccines, especially in connection with the pump

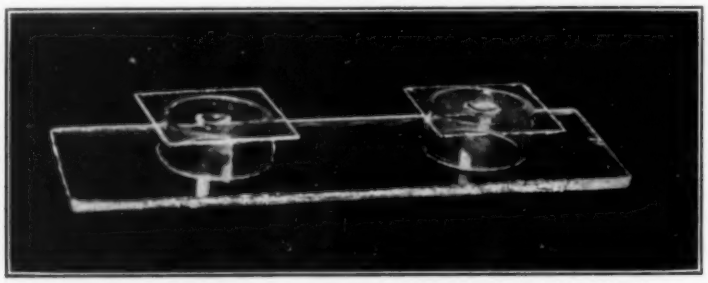

Fig. 6.—Hanging-drop arrangement.

mentioned above. These pipettes are easy to make, and can be made over a Bunsen burner from ordinary glass tubing after a little practice. They are used in separating serum, decanting in washing corpuscles, filling ampules, and the like.

When it is necessary to take a specimen for a blood count and carry it some distance, as for instance from the patient's home to the laboratory, the transportation of the filled pipette without affecting the accuracy of the test

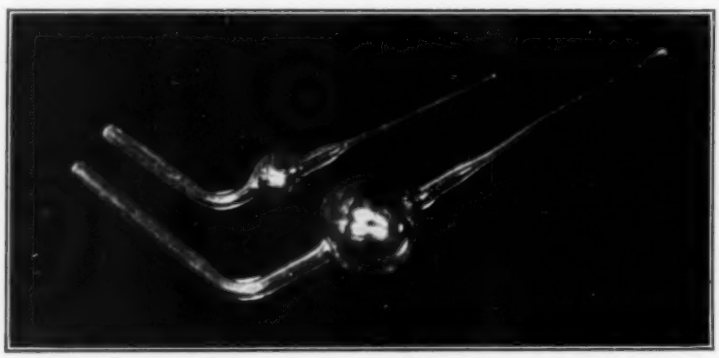

Fig. 7.—Serum pipettes.

has always been a problem. Obviously, the ideal thing is to have a portable microscope, but this is out of the reach of many. I have found that a short piece of heavy inner tube from an automobile tire, forming a heavy rubber band, is an excellent method, the band being placed around the pipette so that pressure is exerted on both orifices.

Another little thing that offers some difficulty for the average practitioner doing his own laboratory work, is the dilution of serum for Widal work. I am

of the belief that this dilution should be made with a fair amount of accuracy; if one merely slaps down a drop of serum and a few drops of water, the test might as well not be done at all. When a large amount of serum is available so that it can be measured in drops or tenths of a cubic centimeter, the dilution is not difficult. The effort should be made to procure a large enough amount of blood; but the fact remains that this is not always done, nor is it always even possible or practical. When only a small quantity of serum is available, it may be measured thus: draw out a glass tube to a long capillary, as much as eighteen inches if possible. Cut off one end at a portion where the bore begins to be uniform; retain the other end as a mouthpiece for blowing out the serum. The serum is allowed to flow in by capillary attraction, for a certain length of the tube measured with a ruler, then the proper quantity of salt solution for dilution, measured by length, taking care to use only that part of the capillary which is of uniform diameter.

None of the apparatus mentioned above is out of reach of the average practitioner, even of the young man starting in practice, either in respect to expense, or skill required in its construction. By conducting efficiently those laboratory operations which he owes as a duty to his patients and himself, he can make the laboratory a pleasant part of his work rather than irksome drudgery.

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EDITORIALS

Measles and Pneumonia in Our Camps

MEASLES and pneumonia are so closely associated in military camps that it is well to consider them together. Measles is one of the most infectious diseases and its restriction in camps seems well nigh impossible except under exceptional conditions when the soldiers can be scattered over large areas. This requires so much housing in the form of tents or barracks, and interferes so greatly with drill and other military activities, that measles is justly greatly dreaded.

The soldier who has had this disease in childhood is fortunate, and a command made up of immunes is doubly so. One attack seems to give life-long protection. It is true that occasionally a soldier, who is sure he has had measles, develops this disease; but it is more than probable that the former attack was due to some other eruptive disease. Organizations recruited from sparsely settled districts are more prone to this infection than those from urban or more thickly settled communities, on account of the larger number of susceptible individuals.

Measles, among our people at least, is seldom fatal so long as it remains

uncomplicated and without more serious sequelæ. This is so generally true that it has been seriously suggested that all susceptibles should be exposed to it in order to secure immunity, but until the complications and sequelæ can be more certainly controlled, this procedure can not be recommended. The control of epidemics of measles is more difficult because it is transmissible before it is recognizable in the individual. This, however, should not deter medical officers from the daily inspection of all men under their charge, and especially of all recent additions to their commands.

On the first evidence of the disease, the soldier should be sent to the hospital and his tentmates should be quarantined for 14 days. This time is believed to cover the period of incubation. The contacts may be drilled in a squad by themselves, but should not be allowed to mingle with others. Their drill master and attendants should be selected from those known to be immune.

A soldier sick with measles should be immediately sent to the hospital, with his clothing and blankets. On arrival at the hospital, the clothing and blankets should be sterilized by steam, rolled in paper, or placed in a paper bag, labeled and put away awaiting the recovery of their owner.

In the hospitals, patients with measles should not be crowded more than is absolutely necessary. However, when the bed capacity is doubled by the number of patients, as has happened in more than one base hospital recently, overcrowding seems unavoidable unless additional cot space can be secured by the immediate erection of hospital tents. When the beds must be brought within four feet of one another, an improvised clotheshorse carrying a sheet kept moist with a 5 per cent solution of carbolic acid, or a 1:1000 solution of bichloride of mercury, should be placed, as a screen, between the cots. This may seem wholly unnecessary, and it might be asked why it is necessary to try to protect one measles patient against another. The purpose of this recommendation is not to prevent the spread of the measles; but some of these patients, experience indicates that many of them, are carriers of virulent pneumococci and streptococci, and the purpose of this precaution is to prevent the dispersion of these virulent organisms. The sputum cups should be burned and the floors should be kept moist and dry sweeping should not be permitted. The patients should be kept warm and given hot drinks. The plates, knives, and forks should be boiled. Drinking cups should not be exchanged, but each patient should have his own. Paper napkins should be used and should be burned with the sputum.

A mistake made in many of our camps is the too early return to duty of soldiers recovering from measles. They should be placed in convalescent hospitals and kept at rest for a period of ten to fourteen days before returning to duty. While uncomplicated measles seldom or never kills, it lowers the resistance to infection with pneumococci and streptococci. Too often it has happened that a soldier returned to duty after recovery from measles is sent back to the hospital within two or three weeks or earlier with pneumonia. On the other hand, in those camps in which the convalescents from measles have had proper care, the number of cases of pneumonia is relatively low. It should be impressed upon every medical officer that a convalescent from measles is especially susceptible to pneumococcic and streptococcic infection, and in order to protect him

from these infections, he should have proper and prolonged professional supervision.

When a soldier recovers from measles and leaves his bed in the hospital, the bedding should be sterilized by steam before it is occupied by another patient. The absence of any provision for this procedure is, up to the present time, a striking feature of most of our base hospitals. Sterilizers, we are told, have been ordered, but up to the early part of December we found no base hospitals fitted with facilities for sterilizing mattresses and blankets. It is claimed by many that exposure for a few hours to the air—we will not say to sunlight because this is by no means always in evidence—is sufficient to disinfect bedding which has been occupied by patients with measles and pneumonia, but some are still skeptical on this point.

That overcrowding has been a factor in the spread of respiratory diseases in our camps seems quite evident. The transmission of these diseases is in inverse ratio to the distance between individuals. With men sufficiently scattered, even measles—as contagious as it is—is not transmissible. The Surgeon-General, with his extensive experience with septic pneumonia in the Canal Zone and in South Africa, has recognized the danger from the respiratory diseases and has insisted from the first that every man in barracks or tents should have a minimum of 50 square feet of floor space. With nine men in a tent 16x16, the space is reduced to less than 29 square feet and in some camps the number of men in such tents was as great as 12. Soldiers have been overcrowded in tents, barracks, and even in hospitals.

The viruses of the respiratory diseases are transmitted for the most part, at least, through the spray present in coughing, sneezing, and rapid talking. It is true that a virulent pneumococcus has been found in dust, and this can not be omitted from the list of distributing agencies. Some of our camps have been very dusty, and how greatly this has contributed to the prevalence of the respiratory diseases can not be accurately determined.

Medical officers should be awake to the danger of overcrowding and should do what they can to avoid it. Line officers have certain valid reasons for preferring compact organizations. It favors administrative purposes. However, there should be no unreasonable conflict on this point among intelligent men, all of whom must recognize the fact that the strength of an army lies in its effective men and is in inverse ratio to those on sick report and in hospital. The medical officer is supreme in the hospital, and still some wards have been overcrowded while others are vacant. Because a ward is intended, in the construction of the hospital for surgical cases, is no reason why it should remain vacant for weeks while the pneumonia wards are carrying twice the number of patients they were built for. If the sterilization of bedding is secured by a few hours' exposure to out-of-door air, a ward should be safe after the removal of all the beds and a few days' exposure with open windows and doors.

In our base hospitals in this country, with no wounded, the greater part of the space, which means the greater number of the wards, should be used for medical cases and especially for respiratory diseases.

It should not be forgotten that overcrowding in sleeping quarters is deter-

mined, to some extent, by the position of the cots with reference to one another. So far as the spread of respiratory diseases is concerned, men may be overcrowded in the open air. It has not been unusual to find men sleeping in cots so arranged that four heads are brought close together. The medical officer should see to the arrangement of cots in tents and barracks. On account of the shortage of blankets and the absence of heating facilities, it is not rare to find two cots brought close together so that the same blankets may cover two men.

It seems to have been assumed by those who had supervision of the housing of our soldiers, that camps and cantonments in the southern states did not need to be warm, and has probably been a contributing factor in the greater prevalence of pneumonia in the southern camps compared with those located in the north. Moreover, it is an old and well certified medical observation that pneumonia is not only more common, but more fatal, in the south than in the northern states. While the average winter temperature in Michigan is lower than that of South Carolina, one may suffer from the cold quite severely in the latter state. The same general idea seems to have prevailed among those whose duty it was to provide winter clothing. This was distributed last in the southern camps, and as late as early December many of the soldiers at Fort Worth, Texas. were not provided with woolen clothing. By one who has experienced the chilling effects of a Texas norther, this defect will be appreciated.

Another mistake in the construction department was to leave the base hospital for the last building to be erected. At Fort Worth, early in December, the base hospital was without running water and sewers, and all bed pans had to be carried a long distance—in some wards as far as a quarter of a mile. There were absolutely no bathing facilities in the base hospital. At Fort Sill, the base hospital was in process of construction, and some of the wards, partially built, were crowded with patients. There were no trained nurses, and the soft coal used in the small stoves was tracked over the floor and the dust was deposited on sheets and pillow cases. In camps and cantonments in this country, the base hospital should be completed, and furnished with every facility, before troops are moved in.

The excellence of the barracks of the aviation corps, and the relative freedom from disease among those occupying them is shown when comparison is made between them and the division housing. It is said that the former were constructed by the aviation corps, not by the quartermaster's department. The construction cost more in money, but, so far, has cost much less in sickness and deaths.

A great sin has been committed in sending troops from a camp known to be badly infected, to one relatively free from infection, without proper precaution. At Camp Wheeler, Macon, Georgia, and at Camp Beauregard, Alexandria, Louisiana, the statement is made that their infection came from Camp Pike, Little Rock, Arkansas. At the last mentioned place, the claim is made that their infection came from Camp Funston, Fort Riley, Kansas. Indeed, the charge is openly made that one camp intentionally emptied its hospital into another camp. While this undoubtedly is a gross exaggeration, there is some truth in these statements. Men have arrived at their destination actually ill with measles,

pneumonia, or meningitis, and have been sent directly from the train to the hospital. Such procedure would not be permitted by civil health authorities. Moreover, this is not the worst of it. Men coming from an infected camp have been immediately distributed among the different organizations at the place of arrival. In this way, the infection has been planted and scattered widely in a most fertile soil. Under no condition, except under the stress of actual warfare, should troops be sent from one camp to another without isolation for a period under medical supervision both before departure and after arrival. This precaution should be taken on all transfers of troops from one camp to another occupied camp. When the movement is from an infected camp, extra precautions should be taken. New arrivals, whether they come from another camp, or from recruiting stations, or directly from their homes, should be quartered apart and inspected individually and daily before distribution among organizations. The transfers of troops should be under the supervision of medical officers, and these should report to the medical officers at the place of destination all infections which have appeared among the arrivals or to which they have been exposed. These precautions might not be necessary among well-seasoned troops who have been in the field for months and possibly for years, but with raw soldiers they are absolutely necessary if infection is to be reduced to a minimum. Within a few months, we should have a constant stream of troops moving from their homes through one camp and another to points of embarkation across the ocean to the battlefields of Europe. To protect these millions from infection, or to reduce infection among them to the minimum, will require the constant attention and care of our most experienced epidemiologists. We can not hope to avoid loss from infection altogether, but we must reduce it so far as possible. We must pay a penalty for the unprepared state into which we allowed ourselves to fall, notwithstanding the warning which came to us so plainly more than three years ago. The seasoned soldier learns to take care of himself, and, if we are correctly informed, the infectious diseases are infrequent among the French and English veterans, but they have had long training. At best, we are to pay dearly for our apathy.

When the new select men are called, each should come to camp with a card from the health officer of his home, giving a list of the communicable diseases observed in that locality during the past month. These men should be housed in groups of not more than 30, and preferably in much smaller groups, kept in quarantine with daily medical inspection for at least two weeks. Their civilian clothes should be disinfected and sent home. The men should have thorough cleaning in supervised baths and under the care of an officer. They should be clothed in proper uniforms and supplied with an extra suit of underclothing. During the period of detention, the men should receive their vaccines and undergo all necessary special medical examinations. Each group, or squad, should be drilled or exercised by itself. At the end of two weeks, groups which have remained free from infection, might be brought together—not more than two groups at first. After shorter intervals, companies may be formed, and finally regiments, but for two months the groups should not be larger than companies. After this, regiments and larger masses may be organized. In the

primary training camps, the arrangement should be such that each company could be isolated from every other part of the camp at short notice. Medical officers especially skilled in the recognition and effective management of communicable diseases, should daily examine every man, stripped and while in his bath. Daily bathing should be a routine exercise. Medical officers, during this preliminary period, should live with the men, eat at the same mess, sleep in the same quarters, and should, at the end of that time, have some voice in the selection of noncommissioned officers. Besides, success in this work should be given weight in fixing the rank of medical officers. All the camps and cantonments now in this country should be maintained at least as long as the war lasts. This is recommended in order that overcrowding may not again be necessary, and, if the number now existent is not enough to prevent overcrowding, more camps and cantonments should be provided. The barracks and base hospitals now in existence should be painted and kept in repair. This should include the water supply, sewerage, baths, etc. Let us proceed as though we expect the war to continue indefinitely. When it does stop, these camps and cantonments may be used for the universal military training for which it is to be hoped we will be wise enough to provide. Some of the base hospitals would be excellent for tuberculosis sanatoriums, if kept in repair. There is nothing more demoralizing to camp sanitation than the idea that the camp is soon to be abandoned.

With the restriction of the death rate from tuberculosis, pneumonia is fast winning the rank of "Captain of the hosts of death." There is a general impression that it is most prevalent among children and the aged, but Cole states that more than half the cases fall between 20 and 50 years—the period of greatest activity. It was the most serious disease met with by the Surgeon-General in the Canal Zone and he was called to South Africa to advise concerning its restriction among the miners in the Rand region. With the exception of dysentery and typhoid fever, pneumonia caused more deaths among the soldiers of the Civil War than any other disease, and with the elimination of typhoid fever, pneumonia in all probability will claim more deaths in our army than any other disease. Experience shows that it is especially prevalent among recruits. It levies a heavy tribute upon those who are passing through the transition from home life to that of the soldier. Many fall its victims in the process of being adapted to the altered conditions of life. Especially is this true when the period of this transition is accompanied by exposure to unusual cold and wet. The fact of this greater prevalence and fatality among the inhabitants of our southern states, has already been mentioned, as has the special susceptibility of those convalescent from measles.

It is customary to speak of lobar and bronchopneumonia. This distinction is useful from the standpoint of the pathologist, but how useful it is from an etiologic or epidemiologic viewpoint remains to be seen. Both forms may be primary and both may follow measles. It is generally believed that lobar pneumonia is more frequently primary, while bronchopneumonia is the form most likely to follow measles. However, up to the present time there are no convincing statistics on this point. It is highly desirable that accurate observations should be made and recorded in our base hospitals as to the relation of the two

forms of pneumonia to measles. The records should show in each case as to whether it was lobar or bronchopneumonia, but what is of more importance, whether it was primary or post measles pneumonia. With accurate observations on these points, properly recorded, we should soon have information of great value in an epidemiologic way, and this is what we greatly need in our efforts to reduce the incidence of these diseases.

Cole defines lobar pneumonia as follows: "Acute lobar pneumonia is an acute infectious disease, the characteristic feature of which is a uniformly diffuse exudative inflammation of entire portions of one or more lobes of the lung. It has long been a question of dispute, however, whether the definition of the disease shall be based on the pathologic, etiologic, or clinical features. In our opinion, so far as prevention and cure of the disease are concerned, it is of the greatest importance that the chief stress should be laid on the etiologic agent. Lobar inflammation of the lung may undoubtedly be caused by a number of different bacteria. The vast majority of the lesions, however, are caused by varieties of diplococcus pneumoniæ."

The bacteriology of bronchopneumonia has not been so completely studied, but it is safe to say that the varieties of bacteria found in the exudate are more numerous, and, while the pneumococcus may be the sole causative agent, streptococci are more frequently present than in lobar pneumonia and may be the chief, if not the sole, causative agent. Careful observation and records in the laboratories of our base hospitals should give us most desirable information concerning the bacteriology of both forms of pneumonia, and there is opportunity in each of these laboratories to make useful contributions to the etiology and epidemiology of pneumonia.

The pneumococcus was first found by Pasteur in the saliva in a case of rabies, and about the same time by former Surgeon-General Sternberg in the normal saliva. The fact that many people in health carry these organisms in their saliva more or less constantly, led to the belief that pneumonia results from the lowered resistance of the individual induced by unusual exposure to wet and cold, an attack of measles, etc., and that isolation and disinfection of sputum was unnecessary. Under this attitude toward the disease, it has not decreased and there is strong evidence that it has increased. The census of 1900 made it responsible for more than 10 per cent of all deaths.

The painstaking investigations of Cole and his associates at the hospital of the Rockefeller Institute have shown that pneumococci may be differentiated into several types and subtypes. This work is still incomplete, but it has progressed far enough to throw much light on the etiology of lobar pneumonia, and to justify us in taking quite a different view concerning the methods that should be followed in attempts to limit the spread of the disease. In a study of the mouth secretion of 297 individuals in health and without history of recent contact with a case of lobar pneumonia, 181 were found to be free from any form of the pneumococcus, while 161 showed some form of this organism. This indicates that more than half of normal individuals, without recent exposure, are free from pneumococci. In the 161, the types were distributed as follows: .

Type I — 0.8 per cent	Type IIb— 5.8 per cent
Type II — 0.0 per cent	Type IIx—11.6 per cent
Type IIa— 0.8 per cent	Type III —28.1 per cent

Type IV —59.9 per cent

In 458 cases of lobar pneumonia, the distribution of the types was quite in contrast with the above as shown by the following:

Type I —33.3 per cent	Type IIb— 0.9 per cent
Type II —29.3 per cent	Type IIx— 2.0 per cent
Type IIa— 1.3 per cent	Type III —13.0 per cent

Type IV —20.3 per cent

"Comparison of these two tables shows that the pneumococci most commonly found in the mouth secretions of normal individuals give rise to a minority of the cases of lobar pneumonia. The disease produced by these organisms, with the exception of Type III, is less severe in character, indicating a lower grade of pathogenicity of those types for man. On the other hand, Types I and II cause a majority of cases of lobar pneumonia, are of high virulence for human beings and are seldom or never found in the mouth secretions of normal individuals who have not been in intimate association with cases of lobar pneumonia. This seems to indicate that lobar pneumonia due to Types I and II does not rise from infection with a pneumococcus which is habitually carried in the mouth, but that infection with these organisms occurs from without."

Men trained by Cole and familiar with his methods of differentiating the types of pneumococci have been placed in the laboratory of each camp in which pneumonia prevails, and we may expect much new information along this line. Cole has developed a serum which apparently gives good results in those pneumonias due to Type I. This serum is being used in cases shown to be due to this type. However, we are at present more deeply concerned with the prevention than the treatment of these diseases, and in our efforts at prevention we are proceeding on the assumption that pneumonia is a transmissible disease, and that the causative agent at least in a large percentage of cases comes from without. In doing this the probability that susceptibility may be increased by unaccustomed and untoward conditions of life must not be overlooked. Indeed, the truth of this is indicated quite conclusively by observations extending back for centuries and recognized in many parts of the world.

We may laud the advantages of free ventilation, out-of-door living and sleeping, the hardening and bracing effects of cold weather, cold bathing, etc., as much as we please, but we must admit that when men in masses suddenly change their residence from warm, unventilated or poorly ventilated homes, to the life of the tent and the open barrack, they need warmer clothing and heavier bedding, and if these are not furnished, pneumonia takes heavy toll from their ranks. Furthermore, it seems true that the more radical and sudden this change, the greater is the toll. The Michigan lad may have his snow bath or his plunge through the broken ice, and quickly get back into his heavy woolens with impunity, but when the South Carolina youth indulges in such an experience and goes back into his cottons, insurance on his life ceases to be a good risk. The French have found it absolutely necessary to provide warmer quarters and heavier

clothing in the winter for their African contingents than is needed by the native Frenchmen.

Hookworm infection among the southern select men has been suggested as an explanation of the lesser resistance they show toward respiratory diseases. It may be a fact, but so far this has not been demonstrated. These facts long known to medical men seem to have been without the ken of those who provided or failed to provide quarters and clothing for the recent recruits in the southern camps. It is for the future to determine whether the Cracker from Georgia will make as hardy a soldier as the Wolverine from Michigan. Both bore many privations in the Civil War and proved themselves worthy antagonists.

To the suggestion that lack of suitable clothing has been a factor in the prevalence of pneumonia in the camps, the reply is made that warm garments in sufficiency are now in the camps or on the way to them. To the man who died of pneumonia in the base hospital in Fort Worth last month, last week, or yesterday, this reply is of small comfort. However, this is no time to look backward, but it is the time to look forward and to see that mistakes are not continued. It is the duty of the medical officer to protest repeatedly and vigorously, if necessary, through official channels, if those under his care suffer from insufficient clothing or bedding. It is also his duty to see not only that they have proper clothing, but that they wear it.

That overcrowding favors the dissemination of pneumonia can not be questioned. It multiplies the number of those within the infection range, increases the contacts and makes segregation more difficult.

On entering an amusement or assembly hall in one of our cantonments and hearing many coughing and filling the air with germ-laden spray, one can not easily dismiss the impression that these places serve as distributors of the respiratory infections. A like impression has evidently been made upon those in authority, for in several camps places of assembly have been closed and similar extra cantonment picture shows have been barred to the soldier. This procedure is regrettable but nevertheless commendable. In the process of making soldiers, some pleasures must be curtailed.

The soldier sick with pneumonia, either primary or post measles, should be immediately carried to the base hospital, and, so far as protective measures are concerned, should be treated much the same as has been recommended for those with measles. Overcrowding in hospital and the screens between beds should be remembered, the one to be avoided and the other to be provided. An individual with Type I of the pneumococcus may distribute his more fatal infection to a neighbor originally infected with the less virulent Type IV, or a streptococcus infection may be engrafted on a pneumococcus growth. The fact that empyema frequently develops in both lobar pneumonia and bronchopneumonia suggests that the streptococcus is present, either as a primary or secondary factor. Moreover, in several hospitals pneumonia has developed in physicians and other attendants. Whether patients with pneumonia do better in a cold or in a warm, moist atmosphere seems to be an undecided question. While this is being determined, it is quite certain that whatever the temperature of the inhaled air may be, the body should be protected from chill. Among those most

experienced in the treatment of pneumonia, the value of digitalis seems to be conceded, but there are differences in opinion as to the extent to which this drug should be administered, as to the indications for pushing or decreasing its administration, and as to the preparation of this drug most suitable.

Inspection of our camps and their hospitals leaves one with the impression that so far as their medical personnel is concerned, the greatest need is for men skilled in the early recognition and the handling of the acute respiratory diseases. Valuable as improvements in the determination of the types of the pneumococcus and the development of curative serums are, the prevention of infection and the limitation of its spread are far more important. The daily mail of the Surgeon-General's office brings suggestions, recipes and offers to sell to the Government "sure cures" for pneumonia. We can leave the treatment of this disease to the wisely selected medical officers in the base hospitals. What is needed is knowledge whereby we can prevent this disease. However, the mere possession of knowledge is of no value unless it be accompanied by the means necessary for its application. Insufficient clothing, overcrowding in tents, barracks and hospitals, and lack of heat in the houses, have been potent factors in the development of the pneumonia among our soldiers, and for these deficiencies the medical corps is not responsible. This is not intended as a criticism on anyone, nor does it imply that the medical corps would have done better if it had been given authority in all these matters. It does mean that in the making of an army, the health of the soldier is of first importance and this can be secured only by the intelligent cooperation of all those who are responsible for the conditions under which he lives.

The Surgeon-General has asked:

(1) That deficiencies in clothing be made good.

(2) That additional tentage and housing be provided, sufficient to give each soldier at least 50 square feet of floor space.

(3) That a detention camp be established with each division, and in which all arrivals may be kept under medical observation for such time as may be necessary.

(4) That a quarantine camp be established in connection with each division and in which contacts, suspects, and carriers can be isolated and observed.

(5) That, where necessary, tents or other housing should be provided for convalescents.

(6) That unfinished hospitals be hastened to completion, including water, sewers and baths.

(7) Additional nurses, when necessary.

(8) The enlargement and better equipment of the base hospital laboratories where desirable.

(9) The selection and detail of medical officers specially qualified in epidemiology as assistants to the division sanitary inspector.

(10) Provision for laying the dust in certain camps.

(11) Special recommendations indicated by the local conditions at certain camps.

—*V. C. V.*

The Use of Atropine as a Diagnostic Agent in Typhoid Infections

THE British Medical Research Committee has issued a monograph on this subject prepared by Captain Marris. The production of immunity to the typhoid infections by triple inoculation, now compulsory in all armies and largely practiced in civilian life, has not been altogether an unmixed blessing, brilliant as the results have been. The immunity attained is only relative and temporary, and, when infection occurs among the vaccinated, the diagnostic difficulties are greatly increased. The symptoms are generally mild and are often wanting in those features which characterize typhoid infections in the unvaccinated. It is true that a positive diagnosis may be made when the isolation and identification of the infecting bacillus is possible, but reliance upon agglutination tests is not safe.

"The atropine test due to Captain Marris, and now to be described, comes, therefore, at a most opportune time, when every additional aid to the diagnosis of this group of cases is to be welcomed. It will be seen that it has both advantages and disadvantages. Its advantages are its great simplicity, for the test can be performed at the bedside by an intelligent nurse, and the fact that it can be effectively applied earlier in the course of the fever than the agglutination test. A disadvantage is that it does not discriminate between the three types of infection, those due to B. typhosus and paratyphosus A and B respectively."

It is to be noted that these tests were applied to young soldiers and during the period between the fifth and fourteenth days of the disease. There seems no reason why the observations should not hold equally good in civilian practice. They have, however, a scientific, as well as a practical, interest. The results appear to be due to the antagonistic action between the alkaloid and the chemical poison developed in the course of typhoid infection.

"When the human body is so infested by bacilli of the typhoid group as to exhibit typhoid, paratyphoid A, or paratyphoid B fever, a toxin is formed which affects the heart in a peculiar manner; the presence of this toxin can be detected by observing the abnormal yet characteristic reaction of such hearts to certain drugs, notably atropine."

The principle of the test seems to depend upon the following known facts:

1. Under ordinary conditions the administration of atropine markedly increases the rate of heart beat.

2. Bradycardia is generally observed in typhoid infection.

3. In this infection the administration of atropine fails to increase the heart beats proportionately to the increase observed in health or in other diseases.

The application of the test is as follows:

"The patient lies horizontally and is instructed to remain completely at rest throughout this test, which is not employed until at least one hour has elapsed from the last meal. The pulse rate is counted, minute by minute, until it is found to be steady; ten minutes of such counting usually suffices. Atropine sulphate is then injected hypodermically in the dose of $\frac{1}{33}$ grain, preferably over the triceps region to insure rapid absorption. An interval of 25 minutes is allowed to elapse,

and the pulse is again counted, minute by minute, until it is clear that any rise which may follow the injection has passed off; 15 or 20 minutes may be necessary for this purpose when the pulse rate is raised at the first count."

For instance, the average before the injection is 68 and that after the injection is 94, giving a difference of 26 beats. In this case the conclusion is reached that the infection is not typhoid. When the increase is not greater than 14 beats, typhoid infection is indicated. In the first instance the reaction is said to be negative, and in the second, positive. Experience fixes the upper limit of a positive reaction at 14 beats per minute and the lower limit of a negative reaction at 15 beats per minute.

"If the patient is admitted during the first fortnight of his illness, the test is applied as soon as possible after admission and is charted with the temperature. When a positive reaction (little or no response to atropine) is obtained, the diagnosis of infection with a member of the enteric group of organisms may be made. In the case of a negative reaction, the test should be repeated after two or three days, and, if again negative, it is again repeated. Three negative reactions falling within the first fortnight of the illness exclude the presence of typhoid with a considerable degree of certainty; there are rare exceptions and in these a continuation of the test is usually suggested by the symptoms and remaining clinical signs."

True cases of typhoid group which are admitted after the fourteenth day frequently yield positive reactions, but negative reactions after this period of illness are often unreliable.

The effect of $\frac{1}{33}$ of a grain of atropine sulphate in the normal individual is as follows:

A slight and short fall in pulse rate is usually seen, and this is followed by a steep rise within ten minutes of the injection; the rise is constant, and is rarely less than 20 beats, and is frequently as much as 30 beats per minute in extent. It reaches its maximum at about 30 minutes, is maintained for varying periods, and then gradually subsides, reaching normal after an hour or more. Dryness of the mouth occurs soon after the injection. Dilatation of the pupil does not always appear but usually occurs after the lapse of an hour or more. A rise of blood pressure may be present, but is insignificant, being usually no greater than 5 or 6 mm. of mercury.

It may be desirable to report that this test has so far been used solely on soldiers who have previously been inoculated, and in whom typhoid is modified. As a rule the course of this modified typhoid is mild, the death rate not being more than 2 per cent. Of the symptoms the author writes:

"The patients are listless; there is mental hebetude; but delirium and the 'typhoid state' are rare. The face is flushed, the conjunctiva conjested, and the expression one of fatigue. The tongue is moist and often furred, but its appearance can not be regarded as characteristic. The pulse is slow, soft, but of fair volume; it is not often dicrotic. The heart's apex beat is ill defined or absent; the sounds are clear, but distant. The abdomen is tumid or doughy and usually a little tender, especially in the left hypochondrium. The spleen may or may not be palpable. The eruption is infrequent, but it may be seen as isolated rose spots or rarely as a rash of protean character. The abdominal reflexes are generally

absent. Over the lungs moist sounds are frequent; signs of some consolidation, more often at the right base than the left, are not infrequent. The temperature may vary considerably, the course may be afebrile from admission, or from a day or two subsequent to admission; in some cases the curve falls abruptly to normal within a few days of admission and remains there, a type which is especially frequent when there have been signs of consolidation of the lungs. It may fall by lysis, ending relatively early at or about the tenth or fourteenth day of the disease. Spiky charts with evening rise and irregular charts resembling those of trench fever are not uncommon. Relapses and complications are comparatively rare."

In 111 cases in which the diagnosis was determined by blood cultures the atropine test was reliable in 98 per cent. The average pulse rise in these cases was 6.6 beats per minute. In 247 cases, diagnosed as typhoid infection by agglutination test, the atropine test was positive in 222.

The atropine test proved positive in a few individuals within from one to three days after typhoid inoculation.

The author attributes the atropine test to antagonistic action between this alkaloid and the typhoid poison on the inhibitory mechanism of the heart. There is no systemic antidotal value in atropine in typhoid fever and this drug is of no value in the treatment of the disease.

—*V. C. V.*